

STUDIES ON DEEP VENOUS INSUFFICIENCY

By

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This thesis is based on the following publications:

- I. After-exercise thermography and prediction of deep vein thrombosis.
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- II. After-exercise thermography compared to strain-gauge plethysmography and venous pressure measurements to detect deep venous insufficiency.
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- III. Deep venous insufficiency after postoperative thrombosis diagnosed with ^{125}I -labelled fibrinogen uptake test.
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- IV. Venous function five to eight years after clinically suspected deep venous thrombosis.
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- V. Venous function after fracture of the lower extremity. A follow-up study eight to ten years after injury.
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- VI. Late venous function of the leg after deep venous thrombosis occurring in relation to pregnancy.
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These papers are referred to in the text by the Roman numerals given above.

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INTRODUCTION

Deep venous insufficiency (DVI) can be defined as impairment of function in the deep veins caused by obstruction or insufficiency of the venous valves. DVI can lead to serious clinical problems with chronic leg swelling, induration of the skin, eczema and venous leg ulcer. It has been known for a long time, that DVI often is a sequel of a deep venous thrombosis (DVT). In recent years, however, it has become apparent that DVI can develop without history or signs of earlier DVT. A symptomatic DVI has often been called a postthrombotic syndrome, an incorrect name, as it can obviously develop without earlier DVT.

There is often a delay between damage to the deep veins and onset of clinical symptoms or signs of DVI. With the introduction of new diagnostic methods, venous physiology has become better understood and today there are methods to diagnose DVI in the stage, where it still does not give clinical symptoms. The true incidence of DVI in the general population is not known, and there are different opinions expressed in the literature about the frequency of DVI following DVT of different extension in the leg and in different types of patients.

The main purpose of this study was to evaluate the frequency of objectively diagnosed DVI after different types of DVT and conditions predisposing for DVT, and to compare it with the frequency in apparently healthy legs.

DVI - HISTORICAL ASPECTS

The association of leg ulcers with disease of the veins of the lower leg has been known since ancient times.

Hippocrates (460-377 B C) noted the association of varicose veins and leg ulcers and also described the use of compression bandages for treatment of these ulcers. Not until Harveys discovery of the circulation of the blood in 1628, and his conclusion that to-and-fro movement of blood is not possible in vessels containing valves, a more profound understanding of venous disorders was established (Anning 1976).

Wieseman (1676) seems to have been the first to realise that ulcers might be due to a circulatory defect, rather than a result of a static condition. Gay (1876), in an investigation of leg ulcers, pointed out that severe long-standing varicosity may exist without ulceration, and that it is, in fact, the rule rather than the exception. He concluded that leg ulcers are a consequence of conditions of the venous system of which varicosity is not infrequently a complication. He also believed that thrombosis might be a cause of venous ulcers.

The first known illustration of a postthrombotic leg is assumed to have appeared in a French book in the 13th century and the first clinical description of postthrombotic conditions come from the English court during the 16th century. Both Henry VIII and Mary Stuart are supposed to have had serious deep venous insufficiency, Mary as a consequence of a postpartum thrombosis. The first detailed description of a postthrombotic condition was made by Charles White in 1784 who called it "postpartum edema" - a hint to the common etiology at that time. The first to relate this condition to thrombosis was John Hunter, who 1794 published a work on "inflammation of the veins" (Haeger 1968).

In 1917 Homans presented his classical study of the patholo-

gy of thrombosis of the deep veins of the leg, still a basis for our present understanding of DVI. He showed that recanalisation with destruction of valves was common after DVT, and that ulcers of the leg followed and were closely related to this deep venous pathology. He also stressed the time factor - sequelae after thrombosis increase with time (Hommans 1917).

The introduction of venography by DosSantos (1938), and in Sweden by Bauer (1942), made it possible to visualize the changes in the deep veins after thrombosis. With the introduction of venous pressure measurements in the leg by McPheeters et al (1932) a functional assessment of the deep veins could be made.

With the help of these new methods, objective studies of DVI could be carried out. In Sweden Bauer was the pioner in this field. He demonstrated that insufficiency of the deep veins and leg ulcers were common after an earlier thrombosis and that the frequency of complications, both subjective, clinical and objectively measured increased with time.

DVI - INCIDENCE AND FREQUENCY

The incidence of DVI in a population is difficult to establish mainly because of three different factors (Gallus 1983):

- 1.-The long delay which frequently intervenes between the initial thrombosis and the full development of clinical symptoms. As a result most studies on this subject are retrospective.
- 2.-In many studies only clinical criteria have been used to define the initial thrombosis with their well known lack of sensitivity and specificity.
- 3.-Many patients with varicose veins may have symptoms from these mimicking DVI.

Another factor may be added:

- 4.-DVI can occur without previous known thrombosis, probably as a result of aging of the venous valves which can make them insufficient (Kistner 1980).

Gjöres (1956) made a careful estimation of the postthrombotic problems in the general population in Sweden. He sent questionnaires concerning leg symptoms to 15 980 randomly selected adults in six widely scattered districts in Sweden. Among the 13 740 responders (86%) 1 453 were examined and interviewed because they gave replies suggestive of past thrombosis or present DVI. 303 (2,2% of the responders) were finally thought to have had a DVT 1-35 years earlier based on history and, in 74% of the cases, on referral to the case notes of the acute episode. 50% of these 303 subjects had intermittent swelling, 39% chronic swelling, 27% induration of the lower leg, 29% leg ulcers and 61% leg discomfort of some kind. One or more symptoms were present in 285 individuals (2,1%). Even if it is assumed that all non-responders had normal legs the minimum incidence of one or more postthrombotic symptoms among adults in this population was 1,8%. It should be noted though, that this investigation was concerned with sequelae of DVT and not DVI per se.

In a study from Basel chronic venous insufficiency was found in 15% of 4 529 persons and venous leg ulcer in about 1% (Widmer 1978). In the Tecumseh (Michigan) Community Health Study Coon et al (1973) found active or healed venous leg ulcer in about 0,5% of 9 226 adults aged over 20. Half of these were estimated to be postthrombotic. In a health study in Skaraborg County, Sweden, (Hallböök 1978) a rising incidence of venous ulcers with increasing age was found. The incidence in persons older than 60 years was about 2%, while venous ulcers were very uncommon in persons under 40. The total population studied was 5 625.

No study exists where a large population has been screened for DVI with objective test methods, and thus the true incidence of DVI in the general population is unknown.

The frequency of DVI after different types of DVT and the influence of certain factors on the development of DVI has been much discussed.

The time-factor is important for symptoms of DVI to develop. The onset of symptoms is usually slow. The full clinical syndrome of DVI has often not developed until ten or more years after venous damage (Bauer 1942, Gjöres 1956, Gallus 1983). Bauer (1942) found that five years after symptomatic DVT 45% had induration of the skin of the lower leg and 20% leg ulcer. After 10 years the figures were 72% and 52% respectively. Objective signs of DVI usually develop long time before the clinical manifestation of the disease. After a thrombosis the process of recanalisation should have taken place before objective assessment is performed, and this process often takes 3-4 years (Bergvall & Hjelmstedt 1968).

It has been claimed that a more extensive DVT is more often followed by DVI. Zilliacus (1946) found severe clinical

signs of DVI after three years in 13% of 46 patients presenting with symptoms of calf vein thrombosis, as compared to 58% of 43 patients with symptoms of thigh vein thrombosis. All patients had been treated with heparin. Bieger et al (1976) reported similar results. 3/35 (9%) of patients with symptoms of calf vein thrombosis and 9/16 (56%) with thigh vein thrombosis had severe symptoms of DVI after 2,5-4 years. Lawrence & Kakkar (1980) found, with an objective test method (foot volumetry), that 77% of 34 patients with major DVT and 16% of 79 patients with calf vein thrombosis had severe hemodynamic changes as in DVI. Their observation time was 2 years. Browse et al (1980), on the other hand, could not show any correlation between the phlebographic extension of the DVT and late symptoms and signs of DVI. Their observation time was 5-10 years.

The importance of the popliteal valve in development of DVI has often been pointed out. Bauer (1948) thought that the popliteal valve was of utmost importance, and this made him operate patients with severe symptoms of DVI with ligation and resection of the popliteal vein. The operation gave good immediate results but was not satisfactory in the long run (Lindhagen & Hallböök 1982). Shull et al (1979) found that the most important factor determining the development of ulceration in earlier thrombosed legs was the condition of the popliteal valve. Ulceration did not occur, even in the presence of occlusion of the femoral vein, if the popliteal valve was competent. Strandness (1983) also demonstrated the importance of the popliteal valve in development of symptomatic DVI.

DVI occurring after DVT during pregnancy has been considered frequent, but has hitherto not been studied with objective test methods.

The frequency of DVI after asymptomatic DVT detected with sensitive screening methods (e.g. ^{125}I -fibrinogen uptake test (FUT)) has so far been poorly documented. Only one stu-

dy exists where DVI after a FUT-detected DVT has been objectively documented (Bergqvist & Hallböök 1979). Five of 50 patients had abnormal strain-gauge plethysmography three years after a FUT-detected thigh vein thrombosis, but the presence of valve insufficiency was not studied. A few studies have been presented where clinically detected DVI after FUT-detected DVT is reported. Browse & Clemenson (1974) found, 3,5 years after postoperative DVT detected with FUT, swelling in 23% of FUT-positive legs as compared to 11% in FUT-negative legs. Aches and pain was present in 21% and 8% respectively. Hedlund (1975) found clinical DVI in two of 70 patients with FUT-detected postoperative thrombosis 30 months earlier. Mudge & Hughes (1978) reported clinical evidence of DVI in 11% of FUT-positive legs and 7% in FUT-negative legs three years postoperatively.

The frequency of DVI in legs at high risk of developing DVT has been studied in a few investigations concerning patients with earlier fracture. Miehle (1982) found in legs with previous open tibial fracture a 40% frequency of clinically detected DVI and Willen et al (1982) reported a 21% frequency of objectively measured DVI (doppler examination) in legs with earlier tibial fracture.

DVI can also occur in legs without previously known DVT. Browse et al (1980) noted in 47 patients with normal phlebography (performed on suspicion of DVT) 5-10 years earlier a frequency of 32% with symptomatic DVI. In a group of patients with unilateral DVT 6-54 months previously, Halstuk et al (1984) found a frequency of 50% with objectively diagnosed DVI (Doppler examination and strain-gauge plethysmography) in the initially healthy leg.

When dealing with patients with different risk conditions for the development of DVI, it must be considered important to compare the risk leg with the contralateral leg, a fact which has previously not been properly paid attention to.

DVI - PATHOPHYSIOLOGY

DVI is impaired function of the deep veins, either as a result of obstruction, or as a consequence of malfunction of the venous valves. Obstruction follows a thrombus that is not recanalised, or pressure from the outside. Valvular insufficiency can be caused by destruction of the valves by a thrombus, due to aging of the valves which make them incompetent or due to hereditary absence of valves.

Venous thrombi are soon covered with endothelial-like cells and invaded by capillary sprouts from the vein wall. Organisation is accompanied by retraction of partly occluding thrombi, or the opening of cell-lined clefts or pockets in totally occlusive thrombi. These processes can lead to partial or complete recanalisation (Hume et al 1970, Sevitt 1973). Small valve-pocket thrombi often spare the valves (Sevitt 1974), while recanalisation of totally occlusive thrombi regularly leads to valve destruction (Edwards & Edwards 1937). The process of recanalisation is slow, and as a rule requires 3-4 years (Bergvall & Hjelmstedt 1968). A return to normal anatomy after an occlusive thrombus is considered unusual (Gallus 1983), while small subclinical thrombi, detected by FUT, probably can dissolve totally (Kakkar et al 1969).

When obstruction remains after a thrombosis, it is often bypassed by collaterals that do not contain valves. This process has been demonstrated in patients subjected to earlier operation with popliteal vein ligation (Lindhagen & Hallböök 1982).

In later years it has become clear that venous valves can become insufficient, not only as a result of thrombosis, but because of aging of the venous wall which makes the valves start to leak (Kistner 1980, Raju 1983). These valves are of special interest as they sometimes can be repaired with reconstructive surgery (Kistner 1980).

Both obstruction and valvular insufficiency lead to impaired return of blood from the leg, and the high pressure can cause a "blow out" of the calf perforating veins directing the blood from the deep to the superficial system (Cockett & Elgan Jones 1953, Linton 1953, Dodd & Cockett 1976). This in turn leads to swelling, especially at the ankle, where the skin becomes prone to ulceration and often shows pigmentation and induration (Dodd & Cockett 1976). According to one theory (Browse & Burnand 1982) the high pressure in the superficial veins distends the local capillary bed and widens the endothelial pores, allowing fibrinogen to accumulate within the tissues and form an insoluble barrier of fibrin. This barrier will impair transport of oxygen and nutrients to the skin cells and can lead to ulceration.

Venous claudication can occur in chronic iliac vein obstruction, but not as a consequence of valvular insufficiency. The pain felt at exercise seems to be the result of a high intramuscular pressure and could be looked upon as a type of compartment syndrome (Qvarfordt et al 1984).

DVI - SYMPTOMS AND SIGNS

The symptoms and signs of DVI have been described by, among others, Bauer (1942) and Dodd & Cockett (1976). They can be summarized as:

Symptoms:

1. Swelling of the ankle and calf.
2. Aches and pain in the calf, especially at exercise.
3. A feeling of heaviness of the leg.
4. Nightly cramps of the leg.
5. Venous claudication.

Clinical signs:

1. Oedema of the lower leg.
2. Pigmentation and induration in the "gaiter area".
3. Eczema of the lower leg.
4. Venous ulcer.

Venous claudication (the regular onset of bursting calf pain with exercise) is an uncommon but characteristic symptom of DVI (Negus 1970).

According to Dodd & Cockett (1976) symptoms are related to the original extent of the DVT. A DVT located below the inguinal ligament produces swelling, induration and leg ulcer, while an isolated iliac thrombosis produces more aches, pain and venous claudication, but less oedema and seldom leg ulcer. The combination of symptoms will occur after DVT:s located on both sides of the inguinal ligament.

DVI - OBJECTIVE DIAGNOSIS

The available objective methods which have been suggested for the diagnosis of DVI are:

1. Phlebography.
2. Venous pressure measurements.
3. Plethysmography of various types.
4. Doppler ultrasound.
5. After exercise thermography.

Phlebography

Phlebography was introduced by Dos Santos (1938) who described the results of ascending phlebography, and the method was introduced in Sweden by Bauer (1940). Bauer (1942) also described the phlebographic findings of sequelae after DVT. Retrograde phlebography was described by Luke (1943).

The diagnosis of postthrombotic changes and DVI and different sources of error have been considered by, among others, Bauer (1942), Højensgård (1951) and Greitz (1955).

Retrograde phlebography can be helpful as a test of valvular function (Gullmo 1963, May & Nissl 1959) but has drawbacks, as full cooperation of the patient is needed, and results may be difficult to interpret.

Phlebography is a valuable method in the diagnosis of DVI, but it mainly reflects anatomic features and gives less information on the functional state of the venous system. It is also an invasive method, and it has been claimed that the injection of contrast into the veins can, per se, induce a high percentage of thrombosis (Albechtson & Olsson 1976), although this concept has been doubted (Kristiansen et al 1981, Berge et al 1981). Furthermore, puncture of a dorsal foot vein may be difficult in patients with DVI, due to skin changes and swolleness.

Venous pressure measurements

In 1910 Moritz & Tabora described a technique for venous pressure measurements in the arm and the first measurements in the leg was reported by McPheeters et al (1932). Reports on venous pressure measurements have since been numerous (e.g. Pollack & Wood 1949, DeCamp et al 1951, Arnoldi & Linderholm 1968) and have greatly aided in the understanding of the pathogenesis of DVI and other venous diseases.

Højensgård & Stürup (1949) found that the resting pressure is equal to the hydrostatic pressure at each point in the saphenous system and Højensgård (1951) stressed the importance of a functional assessments of the venous system. Arnoldi & Linderholm (1968) and Bjordal (1971) have contributed with studies of venous pressure during exercise.

Venous pressure measurements has been considered the golden standard for evaluation of new non-invasive methods determining venous function. Its main draw-back is that it is, like phlebography, invasive, and venepuncture can be difficult in patients with DVI.

Plethysmography

Plethysmography is the oldest non-invasive method for determining venous function. It was first mainly used for evaluation of venous capacity and venous outflow obstruction and used in the diagnosis of acute DVT (Dohn 1956, Dahn & Eirikson 1968, Hallböök & Göthlin 1971). More recently several plethysmographic techniques have been used to study venous insufficiency. Bygdeman et al (1971) studied chronic venous insufficiency and measured venous volume, rate of venous emptying and volume changes with tilting of the patient and were able to determine the degree of reflux. Aschberg (1973) found close correlation between volume increase on tilting (superficial veins compressed) and

clinical findings of DVI.

Barnes (1973, 1984) could calculate the venous reflux flow by passively directing the blood in retrograde direction with tourniquets and found a good correlation with clinical findings of DVI. Norgren (1974) used foot volumetry and found good correlation with venous pressure measurements in patients with DVI. Holm (1976) described a method for ambulatory strain-gauge plethysmography and found good correlation with venous pressure measurements in legs with DVI. Schanzer (1984) has shown good correlation between foot mercury strain-gauge plethysmography and venous pressure measurements and venography in chronic venous insufficiency. Photoplethysmography is another method useful in diagnosis of DVI (Abromowitz 1979).

The great advantage of plethysmographic measurements is that they are non-invasive, correlate well with venous pressure measurements and are quantitative.

Doppler ultrasound

In 1970 Folse & Alexander described doppler measurements for localisation of incompetent perforating veins and found good correlation with operative findings. Lewis et al (1973) reported good correlation between doppler measurements and venous pressure measurements in patients with DVI. Since then, doppler examination has become one of the most important methods for diagnosing venous disease. The method provides qualitative physiological assessment of both venous obstruction and valvular incompetence (Barnes 1982). A bi-directional device can be used and the results recorded on a chart, but non-directional doppler can also give reliable results provided the examiner is experienced (Barnes 1982).

The great advantage of this technique is that it is non-invasive, cheap and correlates well with venous pressure. It gives, however, only qualitative information.

After exercise thermography (AET)

Thermography has been shown to be a valuable screening method for detection of DVT (Cooke & Pilcher 1973, Bergqvist & Hallböök 1978). Henderson et al (1978) reported that a characteristic pattern in thermograms taken after exercise could help to predict the risk of postoperative thrombosis, and Cooke & Pilcher (1974) claimed that an abnormal AET indicated a defective calf muscle pump and thus was a method for detection of DVI. The method was, however, not tested against other objective methods to diagnose DVI.

DVI - DIFFERENTIAL DIAGNOSIS

There are mainly four different conditions to bear in mind in the differential diagnosis of DVI:

1. Venous insufficiency due to superficial venous insufficiency and/or incompetent perforating veins.
2. Chronic leg swelling due to lymphatic obstruction.
3. External venous compression.
4. Recurrent DVT.

Superficial venous insufficiency - perforating veins

Clinical examination is important and often sufficient (Gallus 1983). When the diagnosis is not clear on clinical grounds, phlebography showing normal deep veins is helpful. Measurements of venous hemodynamic changes may be the clue to the correct diagnosis. Venous pressure measurements, plethysmography and doppler examination can be helpful (Negus 1970, Barnes 1973).

Lymphatic obstruction

The diagnosis of chronic lymph stasis is often an indirect diagnosis by demonstrating normal venous anatomy and hemodynamics. The direct diagnosis can be made with lymphangiography.

External venous compression

External venous compression mimicking DVI is usually caused by pelvic malignancies or postradiation fibrosis. Most important is to bear this possibility in mind when examining the patient (Gallus 1983).

Recurrent DVT

Differentiating an exacerbation of DVI from recurrent DVT

can be very difficult. Phlebography and venous hemodynamic measurements are often difficult to interpret. The use of ^{125}I -fibrinogen uptake test can be useful by demonstrating the presence or absence of active fibrinogen deposition at the time of increased leg discomfort and swelling (Wu et al 1974).

DVI - TREATMENT

Treatment of DVI is beyond the scope of this survey and will only be dealt with briefly.

Conservative treatment

Conservative treatment of DVI is based on control of venous hypertension in order to slow down, or prevent, the deterioration of the tissues (Dodd & Cockett 1976). This is achieved by bandaging or with correctly fitted elastic stockings. With an adequate compression very few patients progress to ulceration, even if there is already pigmentation and induration of the skin (Cranley et al 1961).

Pharmacologic treatment with e.g. hydroxyethylrutosides can reduce edema and leg discomfort (Bergqvist et al 1981) but seem to have only marginal effect.

Treatment of leg ulcers is also based on compression as the mainstay of therapy.

Surgical treatment

According to Dodd & Cockett (1976) there are three possible factors in DVI that theoretically can be corrected with surgery:

1. Valve incompetence of the ankle perforating veins.
2. Valve incompetence of the main deep veins.
3. Postthrombotic obstruction of the deep veins.

Surgery of incompetent ankle perforating veins is a well established method, but no controlled trials have been made to evaluate the results (Gallus 1983). However, clinical experience is in favour of the procedure. Recurrence of ulcer after this type of surgery has been estimated to be about 15% (Dodd & Cockett 1976).

In recent years attempts have been made with venous valve reconstructive surgery (Kistner 1980) and venous by-pass surgery or valvular transposition (Bergan et al 1982, Johnson et al 1981). Promising results have been reported (Ferris 1982), but so far the methods have not come into common use.

AIMS OF THE PRESENT STUDY

- to evaluate after exercise thermography as a test to predict legs at high risk of developing postoperative DVT (I) and to test the method against other objective test methods in diagnosis of DVI (II).
- to evaluate the frequency of DVI after asymptomatic DVT (III), symptomatic DVT (IV), DVT in relation to pregnancy (VI) and in legs at high risk of developing DVT (V).
- to compare development of DVI in legs with known DVT with that in apparently healthy legs in the same patient (III, IV, VI).
- to study the influence of DVT with different extension in the leg on development of DVI (III, IV, VI).
- to evaluate the influence of different kinds of prophylaxis against postoperative thromboembolism on development of DVI (III).
- to evaluate the influence of age (III, IV, V) and insufficiency of the popliteal valve (IV, V) on development of DVI.

METHODS OF INVESTIGATIONS

Details of the methods used are presented in each paper and here only a general survey will be given and also a discussion of agreement between the different methods used in our laboratory.

In the studies only objectively diagnosed DVT were considered.

One study (I) was prospective while the other clinical studies (III-VI) were retrospective. In order to avoid that those patients, that could not be reached for follow-up, influenced the results, we analyzed these patients as far as possible and compared them with the patients included in the studies. These results are presented in each paper, and it seems unlikely that the drop-outs have significantly influenced the results. In studies V-VI the patients were obviously aware of which leg that had had DVT/fracture while in study III the patients were not aware of which leg had had DVT. In studies I and II the evaluation of AET was made without knowledge of the results of FUT and objective tests for DVI respectively. In study III the evaluation of DVI was made without knowledge of the FUT-result, while in the other studies the examiner knew the results of phlebography (IV, VI) and side and type of fracture (V) at the time of follow-up.

For symptoms of DVI a questionnaire was used concerning subjective symptoms of venous disorders during the follow-up period and at the time of follow-up. Leg ulcers, swollen legs, discoloration of the legs, eczema of the leg, development of varicose veins, need for compressing bandage or support stockings, nightly cramps and regular use of diuretics were asked for.

Clinical examination included edema, leg ulcer, venous eczema, pigmentation and induration of the leg. Varicose veins

were registered.

The case records for each patient were also reviewed.

"Clinical " DVI was considered present when a patient had, or had had, a leg ulcer. Also patients with at least two symptoms or signs of DVI (swollen leg, discoloration, eczema, nightly cramps, need for compression bandage or support stocking) were considered to have "clinical " DVI.

Concerning "clinical" DVI it could be argued that some of these symptoms might have been due to superficial venous insufficiency and thus the frequency too high. However, in all studies the frequency of varicose veins, both in thrombosed legs and in apparently healthy legs, was about the same. The influence of varicose veins, if any, on "clinical" DVI therefore ought to be of about the same extent in both groups of legs.

¹²⁵I-fibrinogen test (FUT) was used to diagnose DVT (I). FUT is a well established method for detection of postoperative DVT and shows good correlation with phlebography (Negus et al 1968, Browse 1972).

For objective assessment of venous hemodynamic problems many different methods have been described. For detection of venous obstruction doppler ultrasound and various types of plethysmography give reliable results (Dahn & Eiriksson 1968, Hallböök & Göthlin 1971, Barnes 1982 among others).

Detection of valvular insufficiency is a more complex problem. Phlebography can be used, but it is invasive and gives more of an anatomic image of the veins, while the dynamics are more difficult to evaluate. Venous pressure measurements has been the golden standard for many years but has a definite drawback in the fact that it is invasive. Lately doppler ultrasound has become commonly used in detection of venous valvular insufficiency as it is non-invasive, easy to

perform and correlate well with venous pressure measurements (Folse & Alexander 1970, Lewis et al 1973, Barnes et al 1975, Barnes 1982).

To evaluate the methods available in our laboratory a study was made to compare bi-directional doppler with phlebography, venous pressure measurements and non-directional doppler in detection of venous valvular insufficiency.

Study of objective evaluation of venous valvular insufficiency

45 patients (mean age 70 years) with clinical suspicion of DVT five to eight years previously were investigated. In all patients venous pressure measurements and measurements with both non-directional and bi-directional doppler were performed. 44 legs were also investigated with retrograde phlebography.

Venous pressure recordings were performed with a 0,8 mm scalp vein needle inserted into a dorsal foot vein and connected to a pressure transducer. A stasis with slight pressure was applied just below the knee to occlude the superficial veins. The pressure decrease during knee-bendings and the return time (time for pressure to regain pre-exercise value after exercise had stopped) were recorded in mmHg and seconds respectively. A pressure decrease of less than 30 mmHg and return time less than 25 seconds were regarded as abnormal (Pollack & Wood 1949, DeCamp et al 1951, Shull et al 1979).

Doppler examinations were performed with Medsonics Model BF4A, 5,3 MHz, and bi-directional doppler with a Vaso-flo^R (Sonicaid), 8MHz, with built-in pen recorder. For detection of the valve in the sapheno-femoral junction, a stasis was applied just distal to the junction to occlude the great saphenous vein. The probe was placed over the junction and the femoral vein identified. On manual calf-

compression the flow in the femoral vein was noted (with the non-directional doppler by sound and with the bi-directional on the recorder). The stasis was then placed just distal to the knee to occlude the lesser saphenous vein, the probe placed over the popliteal vein, and the same manouvre repeated to record the flow in the popliteal vein (Folse & Alexander 1970, Barnes 1982,).

Phlebography was performed according to the technique advocated by Greitz (1954) and Rabinow & Paulin (1972). Both ante- and retrograde investigations were performed, the retrograde with injection of contrast in the femoral vein and pictures taken while the patient performed a valsalva manouvre. Insufficiency was considered present if the contrast was forced to pass at least two valves and no sufficient valve could be seen distally.

Results of the study are presented in the following tables:

Non-directional doppler compared to bi-directional doppler (90 legs):

a) Investigation of femoral vein valve insufficiency

		<u>Bi-directional</u>		
		Normal	Insuff	
<u>Nondirec</u> <u>tional</u>	Normal	56	2	sensitivity 93,5%
	Insuff	3	29	specificity 95,0%
				accuracy 94,4%

b) Investigation of popliteal vein valve insufficiency

Bi-directional

		Normal	Insuff	
<u>Non-directional</u>	Normal	67	4	sensitivity 80,0%
	Insuff	3	16	specificity 95,7%
				accuracy 92,2%

Venous pressure compared to bi-directional doppler (88 legs):Bi-directional

		Normal	Insuff	
<u>Venous pressure</u>	Normal	41	29	sensitivity 32,6%
	Insuff	4	14	specificity 91,1%
				accuracy 62,5%

Retrograde phlebography compared to bi-directional doppler (44 legs):Bi-directional
doppler

		Normal	Insuff	
<u>Phlebography</u>	Normal	19	15	sensitivity 37,5%
	Insuff	1	9	specificity 95,0%
				accuracy 63,6%

Bi-directional doppler was chosen as the reference method in this study since by showing the retrograde flow it measures the functional state of the valves. It can distinguish between insufficiency in the femoral and popliteal vein, and it can also be registered (Folse & Alexander 1970, Barnes 1982).

Results in this study show that almost as good results can be obtained with a simple non-directional doppler examination with subjective registration of insufficiency, provided the technician is experienced. It is not as time-consuming and easier to use in a screening situation, and it is possible to distinguish between femoral and popliteal valve insufficiency.

Venous pressure measurements seem to give very few false positive results compared to bi-directional doppler but many false negative. This is probably due to the fact that the needle inserted can very easily change position, especially during exercise, and the free flow through the needle is then disturbed. Thus a negative result with this method cannot be relied upon. The main draw-backs are that the method is invasive, time-consuming and does not distinguish between femoral and popliteal insufficiency.

Phlebography also gives many false negative results due to the need for very good cooperation from the patient during the valsalva manouvre. The method is invasive, time-consuming, expensive and cannot show an isolated popliteal valve insufficiency.

As a result of this study the following methods for objective assessment of DVI were chosen:

Strain-gauge plethysmography for detection of deep vein obstruction. Venous pressure recordings and non-directional doppler examination for detection of venous valvular insufficiency. Venous pressure was included, as it is still by

many considered the golden standard of venous hemodynamic studies.

"Objective" DVI was considered present when venous outflow obstruction could be demonstrated with plethysmography and/or venous valvular insufficiency could be demonstrated with venous pressure measurements or doppler examination.

SUMMARY OF INVESTIGATIONS

Details are given within each paper (I-VI).

STUDY I - AET AND PREDICTION OF DVT

In 112 patients undergoing elective hip surgery or abdominal surgery, AET was prospectively used to evaluate this method as a screening method for predicting the risk of developing postoperative DVT. AET was performed according to Henderson et al (1978) preoperatively, and the patients were followed with FUT to detect postoperative DVT. The risk of developing a DVT was 12,8% in legs with positive AET and 11,5% in legs with normal AET. Uni- or bilateral positive AET was associated with a 24,1% risk of DVT as compared to 22,2% when AET was bilaterally normal. All patients recieved prophylaxis against postoperative thromboembolism, but the type of prophylaxis and the type of operation did not influence the frequency of DVT in relation to the results of AET.

Comments:

Much effort has been aimed at finding a method to predict patients at high risk of developing postoperative thromboembolism, in order to select patients in need of prophylaxis. Most trials have analyzed changes in the hemostatic system, but this approach has given little help for routine practise. In 1974 Cooke & Pilcher described a very distinct pattern seen in some patients on thermograms performed after leg exercise. They ascribed this finding to a defective calf muscle pump. In 1978 Henderson et al reported that this distinct pattern could be used for predicting patients at high risk of developing postoperative DVT. They found, after abdominal surgery, FUT-detected DVT in 11% of patients with bilaterally normal AET, 63% in patients with unilaterally positive AET and 92% in patients with bilaterally positive AET. The results were 30%, 56% and 75% respectively in patients after elective hip surgery. All differences were

highly significant.

Our investigation could not verify these results. AET cannot be used for screening patients at high risk of developing postoperative DVT. Our results are not surprising, as DVT is a multifactorial condition, and even if AET could detect DVI, other predisposing factors of DVT are not measured. The results logically led us to the question: Does a positive AET measure DVI? (II).

STUDY II - AET COMPARED TO PLETHYSMOGRAPHY AND VENOUS PRESSURE TO DETECT DVI

In 167 patients AET was compared with strain-gauge plethysmography and venous pressure measurements to evaluate if the specific pattern seen in some investigations with AET could be related to objective tests of DVI. AET was also correlated to subjective manifestations and clinical signs of DVI.

The results showed no correlation between a positive AET and abnormal plethysmography and/or abnormal venous pressure recordings. Neither could subjective manifestations or clinical signs of DVI be correlated to a positive AET. Patients with positive AET had more often varicose veins than patients with normal AET.

Comments:

Cooke & Pilcher (1974) claimed that the very distinct pattern seen on thermograms taken after leg exercise in some patients, was an indication of a defective calf muscle pump and thus indicated DVI. The method was, however, not tested against other objective tests of DVI. The characteristic pattern could be well demonstrated in many patients in our study, but we could not correlate a positive AET to "clinical" or "objective" DVI. Thus AET cannot be used as a screening method for detection of DVI, and it was therefore omitted from the further studies.

The remaining studies deal with development and frequency of DVI after different types of DVT and in patients at high risk of developing DVT.

STUDY III - DVI AFTER FUT-DETECTED POSTOPERATIVE DVT

A follow-up examination was performed in 381 patients who had been operated on with elective hip surgery or abdominal surgery and followed postoperatively with FUT. The aim was to evaluate FUT as an indicator of risk for development of DVI, and also to evaluate the influence of different kinds of prophylaxis against postoperative thromboembolism on development of DVI. As prophylaxis dextran 70, low-dose heparin, low-dose heparin in combination with dihydroergotamine and a heparin analogue, sodium pentosan polysulphate, had been used. There was also a control group where no pharmacologic prophylaxis had been given. Both FUT-positive and FUT-negative legs were investigated. Follow-up time averaged 51 months and mean age at follow-up was 71 years.

No statistically significant differences were found between FUT-positive and FUT-negative legs as regards "clinical" or "objective" DVI. "Clinical" DVI was present in 22% of both FUT-positive and FUT-negative legs and "objective" DVI in 29% and 25% respectively. The extension of the DVT, as detected with FUT, did not affect the frequency of DVI. Although the frequency of postoperative DVT was different in the different prophylaxis groups, the frequency of both "clinical" and "objective" DVI at follow-up did not significantly differ between the groups.

STUDY IV - DVI AFTER CLINICALLY SUSPECTED DVT

154 patients, who five to eight years previously had been subjected to phlebography because of clinical suspicion of DVT, were investigated to evaluate the frequency of DVI. In 75 legs a DVT had been present. Both legs with and without phlebographically proven DVT, as well as not phlebographed

legs, were studied.

There were only minor differences between legs with and without earlier DVT. "Clinical" and "objective" DVI did not differ between legs with positive or negative phlebography. DVI was as common after calf vein thrombosis as after more proximally located thrombosis. High age and incompetence of the popliteal valve were of great importance for development of DVI. No correlation between DVI and impaired arterial circulation was found. About 30% of legs without earlier symptoms of DVT had "objective" DVI at follow-up.

STUDY V - DVI AFTER FRACTURE

150 patients were examined eight to ten years after unilateral, single fracture of the lower extremity (femoral neck fractures not included) to evaluate the frequency of DVI. Both fractured and non-fractured legs were studied.

"Clinical" DVI was more common in the fractured legs than in the non-fractured, while "objective" DVI did not differ between the groups. Only minor differences were noted between legs with different fracture localisation. High age and incompetence of the popliteal valve were more important in the development of DVI than earlier fracture. The frequency of DVI in non-fractured legs was 30%.

STUDY VI - DVI AFTER DVT IN RELATION TO PREGNANCY

A follow-up examination after 3-13 years was performed in 23 women, who had developed a DVT during pregnancy, or the first two weeks after delivery, to evaluate the frequency of DVI. Seven thrombi had been located in the calf while the remaining sixteen extended into the femoral or iliac vein. Nineteen thrombi were left-sided. Both legs with and without earlier DVT were studied.

"Clinical" DVI was presented in eight legs with earlier DVT

(35%) as compared to none in the non-thrombosed legs. "Objective" DVI was present in 15 legs (65%) and 5 legs (22%) respectively. The differences are statistically significant. No correlation between "objective" DVI and extension of the DVT was noted.

In studies III-VI there were altogether 943 apparently healthy legs without history of previous DVT or fracture. These legs were analyzed separately. 22% of these legs had "clinical" DVI and 27% "objective" DVI (Table I). There was an increasing frequency of "objective" DVI with age (Table II). No difference in sex or frequency of impaired arterial circulation was observed between healthy legs with and without "objective" DVI.

TABLE I

DVI in apparently healthy legs

	(III) FUT- neg		(IV) No symp- toms		(V) No frac- ture		(VI) No DVT		Total	
	No	%	No	%	No	%	No	%	No	%
No of legs	625		148		150		23		946	
"Clin."DVI	135	22	50	34	20	13	0	0	205	22
"Obj."DVI	159	25	47	32	44	29	5	22	255	27

TABLE II

Apparently healthy legs

	<u><50 years</u>	<u>50-69 years</u>	<u>> 70 years</u>
No of legs	133	443	370
"Obj"DVI	25 (18,8%)	103 (23,3%)	127 (34,3%)
	└── n.s. ──┘		└── p < 0,001 ──┘
	└──────────────── p < 0,001 ──────────┘		

"Objective" DVI in earlier thrombosed legs (III, IV, VI) was compared and results are presented in Table III. Symptomatic DVT (IV, VI) was followed by a higher frequency of "objective" DVI than asymptomatic DVT (III).

TABLE III

"Objective" DVI in legs with previous DVT

	<u>"Obj" DVI</u>		
FUT-pos (III)	45/135	(29%)	┌── p < 0,05 ──┐ └── n.s. ───┘ p < 0,01
Phlebography pos (IV)	37/75	(49%)	
DVT-pregnancy (VI)	15/23	(65%)	

GENERAL DISCUSSION

Deep venous insufficiency is a common clinical problem. The incidence of postthrombotic DVI in the general population has been estimated to 1-2% (Gjöres 1956, Widmer 1978), but very little is known about the incidence of DVI occurring without previous thrombosis. There are no reports in the literature where a general population has been screened with objective test methods to detect DVI. Thus the true incidence of DVI, both postthrombotic and from other causes, in the general population is unknown.

Little is known about the socioeconomic effects of DVI. Gjörres (1956) reported that 40% of patients with previous DVT were permanently slightly decreased in working capacity, 8% had to give up work and 3% were completely incapacitated mainly due to sequelae of DVI. O'Donell et al (1977) reported socioeconomic effects after iliofemoral thrombosis and found 17 of 21 patients that were essentially invalids due to severe DVI, resulting in high costs of medical treatment and disability payments.

DVI is due either to obstruction of the deep veins or to incompetence of the deep vein valves. This valvular insufficiency is often caused by an earlier DVT, but may also have other causes. Ageing of the valves, weakening of the vein wall resulting in incompetence of the valves and hereditary absence of valves have been discussed (Dodd & Cockett 1976, Kistner 1980).

To get a good estimation of the presence of DVI in a leg, a careful patient history and clinical examination must be combined with objective tests (Aschberg 1973). Clinical diagnosis can be difficult, especially in patients with varicose veins and/or incompetent perforating veins but without deep venous obstruction or valvular incompetence (Aschberg 1973, Gallus 1983).

With objective tests of DVI it must be possible to diagnose both deep venous obstruction and incompetence of the valves in the deep veins. Plethysmographic methods, phlebography and doppler examinations can diagnose venous obstruction. In the present clinical studies (III-VI) strain-gauge plethysmography was chosen mainly because it is well established and a routine method at our laboratory.

To detect venous valvular incompetence venous pressure measurements have, for many years, been considered the golden standard and was therefore included in the studies. There is, however, a risk for incompetent perforating veins to obscure the results of venous pressure recordings, as the distal tourniquet compression is applied above the ankle perforating veins and cannot prevent an outward flow through these perforators (Norgren 1974). The risk does not seem to be high as the study comparing venous pressure measurements to doppler recordings (page 25) shows that only 5% of the legs had a normal doppler recording but pathologic venous pressure measurement. In the clinical studies (III - VI) doppler examination was also used for detection of valvular incompetence, a test that today is considered perhaps the best objective test method, as it demonstrates directly the retrograde flow passing insufficient valves (Barnes 1982). Even if the true frequency of "objective" DVI is somewhat high in these studies, the other objective test methods show that the relation between "objective" DVI in legs with previous DVT/fracture and apparently healthy legs is the same, even if venous pressure measurements are disregarded. Furthermore the frequency of varicose veins did not differ significantly between the groups.

Because of the difficulty to objectively diagnose DVI, a simple screening method has been looked for. When a characteristic pattern in thermograms taken after leg exercise was claimed to indicate DVI (Cooke & Pilcher 1974), and also was claimed to predict patients at high risk of developing postoperative DVT (Henderson et al 1978), studies I and II were

initiated. We could not, however, show that AET had any relation to objectively measured DVI (II), nor that AET could predict postoperative DVT (I).

Development of DVI without earlier known DVT has been reported with a frequency ranging from 7-30% (Yong et al 1974, Mudge & Hughes 1978, Browse et al 1980). The explanation for this has been claimed to be aging of the venous valves which makes them start to leak (Kistner 1980). The present studies show a frequency of "clinical" DVI of 22% and "objective" DVI of 27% in the total material of apparently healthy legs (Table I). This total material is by far the largest reported. There is an increasing frequency of "objective" DVI with age (Table II).

"Objective" DVI was found in 29% of legs with previous sub-clinical DVT (III), in 49% of legs with previous symptomatic DVT verified with phlebography (IV) and in 65% of legs with symptomatic DVT in relation to pregnancy (VI), (Table III). Thus symptomatic DVT is followed by a higher frequency of DVI than asymptomatic DVT.

Most symptomatic DVT had been treated with anticoagulants, while the FUT-detected DVT had not. From the present studies it cannot be concluded if treatment influences the development of DVI. If treatment is effective in preventing DVI, treatment of FUT-detected DVT might have given an even lower frequency of DVI in this group, and untreated symptomatic DVT might have shown a higher frequency of DVI at follow-up. To answer this question, a prospective study comparing treatment versus non-treatment of DVT would have to be performed.

"Clinical" DVI was less common than "objective" DVI. This was expected since there is often a long delay between damage to the veins and onset of symptoms (Bauer 1942, Gjörres 1956, Barnes 1973, Gallus 1983)

FUT is a well established method for detecting postoperative DVT. It shows good correlation with phlebography (Negus et al 1968, Browse 1972) and a positive FUT indicates a risk of postoperative pulmonary embolism (Browse et al 1974, Warlow & Ogston 1973). The frequency of DVI after a FUT-detected DVT has so far been poorly investigated. In a preliminary study we reported a frequency of about 25% DVI in both FUT-positive and FUT-negative legs in 179 patients (Lindhagen et al 1983). One other study is published with objective diagnosis of DVI. A 10% frequency of outflow obstruction was reported in FUT-detected thigh vein thrombosis with plethysmography (Bergqvist & Hallböök 1979). Other studies on this subject have been based on clinical evaluation of DVI (Browse & Clemenson 1974, Hedlund 1975, Mudge & Hughes 1978). In the present study (III) no differences could be noted in frequency of DVI between FUT-positive and FUT-negative legs. Practically all FUT-detected DVT were clinically silent and not treated.

Various opinions have been expressed in the literature about what the extension of a DVT means for later development of DVI. Lawrence & Kakkar (1980), for example, found with objective test methods a higher frequency of DVI after symptomatic thigh vein thrombosis than after calf vein thrombosis. Browse et al (1980), on the other hand, could not find any difference, but used clinical criteria of DVI. In the present studies no correlation between DVI and extension of DVT was noted. However, iliac vein DVT were unusual in our materials, and after symptomatic DVT there was a tendency, although not statistically significant, towards more DVI after DVT of greater extension (IV, VI). We also noted a higher frequency of DVI after symptomatic than after asymptomatic DVT. Thus DVI seems to be more correlated to the DVT giving symptoms, than to the anatomic extension.

A rising frequency of "objective" DVI with age was found in study IV and V, while no such tendency was recorded in study III and VI. However, in study III and VI the range in age

was much smaller, which might explain the results. This increase of "objective" DVI was also observed in all the apparently healthy legs (Table II). The rising frequency of DVI with age is consistent with theories presented by Kistner (1980) about ageing of the venous valves, and by Raju (1983) about a congenital defect in the venous valve tissues in many patients as the basis for ectasia and reflux.

The importance of the popliteal valve in development of DVI has been pointed out many times (Bauer 1948, Shull et al 1979, Partsch et al 1980, Strandness 1983). The present studies (IV, V, VI) show that doppler detected insufficiency of the popliteal valve is more often associated with "clinical" DVI and also with pathologic findings in the other objective test methods of DVI. Leg ulcer was more common in legs with insufficiency of the popliteal valve than in legs with a normal valve (V).

Prophylaxis against postoperative thromboembolism, both with mechanical and pharmacologic methods, can effectively reduce the frequency of postoperative DVT (for review see Bergqvist 1983). How different thromboprophylactic methods influence the development of DVI has previously not been studied. Of the prophylactic methods used in study III, all have been documented as effective in reducing postoperative FUT-detected DVT. Even though the frequency of postoperative DVT differed a great deal between the different prophylaxis groups, the frequency of DVI, both "clinical" and "objective", did not differ significantly at follow-up. Even in the group that had not received any pharmacologic prophylaxis, DVI was as common as in the groups that had. Results indicate that the types of prophylaxis studied do not prevent development of DVI even though the number of FUT-detected DVT's can be reduced. This is well in accordance with the results showing that development of DVI does not differ between FUT-positive and FUT-negative legs. In spite of this, prophylaxis is indicated in many patients as it reduces the frequency of fatal pulmonary embolism (Sevitt & Gallagher 1959,

International Multicentre Trial 1975, Gruber et al 1980, Gruber 1982).

DVT as a complication to fracture of the lower extremity is well known and frequencies from 8-40% have been reported (Jacob 1943, Bauer 1944, Sevitt & Gallagher 1959, Solonen 1963, Culver et al 1970). Damage to the deep veins in association with fractures has been shown phlebographically (Hjelmstedt & Sundström 1963, Nylander & Semb 1972). Only few studies exist where DVI after fracture has been studied. Støren and Auensen (1971) and Miehle (1982) have made evaluations with clinical diagnosis of DVI and a 66% frequency of DVI in legs with symptomatic DVT after hip fracture and a 40% frequency in legs with earlier open tibial shaft fractures were reported respectively. Willen et al (1982) reported a follow-up of 38 patients with previous tibial shaft fractures with doppler evaluation of DVI, and found 21% DVI 13-17 years after injury.

We found a frequency of about 30% of "objective" DVI in both fractured and non-fractured legs 8-10 years after injury (V). The type of fracture did not influence the results (femoral neck fractures were not studied). "Clinical" DVI was more common in fractured than in non-fractured legs, probably because symptoms related to the previous fracture subjectively could not be distinguished from symptoms of DVI. The length of treatment did not influence the development of DVI. This is in accordance with the findings of Hjelmstedt & Sundström (1963). The frequency of "objective" DVI after fracture does not differ from that found in apparently healthy legs in the other studies (III, IV). Thus fracture of the lower extremity (femoral neck fractures excluded) does not seem to predispose to later DVI.

DVT during pregnancy is fairly uncommon. The incidence of thromboembolic complications has been reported to be 2-5/1000 deliveries (Bonnar 1981). In Sweden, in a prospective study, the incidence of symptomatic DVT during pregnancy has been estimated to 0,07% of full term pregnancies

(Bergqvist et al 1983). Although the incidence is low, pulmonary embolism is the second most common cause of maternal mortality in the Western world (Bonnar 1981, Editorial, Br Med J, 1979). The frequency of DVI after a DVT presenting during pregnancy has been considered high (Bonnar 1981), but no studies previously exist where this has been evaluated with objective methods. In study VI "clinical" DVI was found in 35% of legs with earlier DVT, a frequency well in accordance with that found after symptomatic DVT (44%)(IV). "Objective" DVI was found in 65% of DVT-legs. The difference between this figure, and that found in legs with symptomatic DVT confirmed with phlebography (IV), is not statistically significant (Table II). However, the patients are young and are at high risk of disabling DVI during many years. A lower frequency of both "objective" and "clinical" DVI was noted in the non-thrombosed legs as compared to the other studies (III-V), probably due to the patients being young. The DVT in study VI differ from those in study III and IV in that there are more iliac vein thrombi and a great left-sided dominance in the DVT observed in relation to pregnancy. This distribution is also seen in DVT occurring in patients on oral contraceptives (Bergqvist et al 1982).

There are no reports in the literature on the influence of the arterial circulation on development of DVI. In study IV a significantly higher frequency of "objective" DVI was noted in patients with impaired arterial circulation, in spite of the fact that DVT was equally distributed between patients with and without impaired arterial circulation. However, the patients with impaired arterial circulation were significantly older than patients with normal arterial circulation, and within each age-group there was no difference in "objective" DVI between patients with normal or impaired arterial circulation. In the apparently healthy legs (III-VI) no difference in frequency of impaired arterial circulation was noted between legs with and without "objective" DVI. Thus we could not show any influence of arterial circulation on development of DVI. However, the

studies were not designed especially to investigate this problem.

The present study differs from most earlier studies in this field in that we have only accepted objective criteria for diagnosis of both DVT and DVI. We have also made comparisons with apparently healthy legs in the same patient in order to make the results more reliable, and to get a better overall picture of the problems of DVI. Some questions arise from this study that will have to be further investigated: e.g. What is the true incidence of objectively measured DVI in a general population? What influence has treatment for DVT on development of DVI? Is arterial insufficiency a factor in development of DVI? Can early treatment of asymptomatic DVI influence later development of serious symptomatic sequelae? Is the frequency of DVI different after a DVT induced by oral contraceptives than after other types of DVT?

CONCLUSIONS

- After exercise thermography is not useful for prediction of patients at high risk of developing postoperative deep venous thrombosis and can not be used for detection of deep venous insufficiency.
- Objectively measured deep venous insufficiency is more common in legs with previous symptomatic deep venous thrombosis than in legs with previous asymptomatic thrombosis.
- Fracture of the lower extremity does not predispose to development of objective deep venous insufficiency.
- Objectively measured deep venous insufficiency is as common in apparently healthy legs as in legs with previous asymptomatic deep venous thrombosis.
- The extension of a deep venous thrombosis does not influence the development of deep venous insufficiency.
- Pharmacologic prophylaxis against postoperative thromboembolism does not influence the development of deep venous insufficiency.
- There is a rising frequency of objectively measured deep venous insufficiency with age, regardless of previous deep venous thrombosis.
- Incompetence of the popliteal valve is of great importance in deep venous insufficiency.

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AFTER-EXERCISE THERMOGRAPHY AND PREDICTION OF DEEP VEIN THROMBOSIS

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Abstract

A total of 112 patients participated in a prospective study of after-exercise thermography as a screening method for predicting risk of postoperative deep venous thrombosis. The fibrinogen-uptake test was used to detect thrombosis after elective surgery. The incidence of the complication showed no significant difference between patients who had had positive and those who had had negative thermograms.

Thermography does not seem to be useful for predicting risk of postoperative thrombosis.

Introduction

After-exercise thermography shows a highly distinctive pattern in some patients. This pattern has been claimed to indicate deep venous insufficiency.¹ In a prospective study of 109 patients² the pattern was associated with high risk of postoperative thrombosis as detected by the fibrinogen-uptake test. As postoperative thrombosis is a multifactorial condition, devising a simple test to predict this risk presents great problems. We therefore conducted a prospective study to see whether after-exercise thermography in our hands could detect high-risk patients.

Patients and methods

We studied 112 patients (63 men, 49 women) aged 51-86 years (mean age 67.6 years). All were participating in a study of prophylaxis against postoperative thromboembolism. Dextran 70 was given to 53 patients and a combination of dextran 70 and dihydroergotamine to 59 patients. Elective hip replacement was performed in 65 cases and abdominal surgery in 47.

After-exercise thermography was performed preoperatively with the AGA 680 Medical System. A resting thermogram was recorded with the patient's legs 15-20° above heart level after the unclothed legs had been exposed to room temperature for 10-15 minutes. The patient was then instructed to walk around the room or do knee-bends for two minutes. As soon as possible after the exercise a second thermogram was recorded with the patient positioned as before. A network of linear hot spots crossing the anterior tibia, not present on the initial thermogram, was regarded as positive.²

The ¹²⁵I-fibrinogen uptake test was used to detect postoperative thrombosis. The test was performed as described by Kakkar et al³, but with slight modifications.⁴ Measured activity was correlated with the precordial activity. An increase in uptake of 20 % or more as compared with adjacent points on two consecutive measurements was accepted as the criterion for deep venous thrombosis. The thermograms were interpreted by one of us (BL) before knowing the results of the fibrinogen-uptake test.

Results

After-exercise thermography gave positive results in 94 legs in 58 patients. Thus 36 patients had positive results in both legs. The fibrinogen-uptake test detected thrombosis in 27 legs in 26 patients; hence one patient

had thrombosis in both legs. All thrombi were below knee level. Tables I and II summarise these results. The risk of developing thrombosis detectable by the fibrinogen-uptake test was 12.8 % (12/94) in legs yielding positive thermograms and 11.5 % (15/130) in legs yielding negative thermograms. The difference was not statistically significant.

Table I-Results of after-exercise thermography and fibrinogen-uptake test. (Figures are numbers of legs)

Result of fibrinogen-uptake test	Result of after-exercise thermography		Total
	Positive	Negative	
Positive	12	15	27
Negative	82	115	197
Total	94	130	224

Table II-Results of after-exercise thermography and fibrinogen-uptake test. (Figures are numbers of patients)

Result of fibrinogen-uptake test	Result of after-exercise thermo- graphy			Total
	Positive		Negative	
	Unilateral	Bilateral		
Positive	4	10	12	26
Negative	18	26	42	86
Total	22	36	54	112

Positive after-exercise thermograms from one or both legs were associated with a 24.1 % (14/58) risk of postoperative thrombosis, as compared with a 22.2 % risk (12/54) when both thermograms had been negative. The corresponding figures for bilaterally positive and unilaterally positive thermograms were 27.8 % and 18.2 % (table III). None of the differences was statistically significant.

Table III-Incidence of postoperative deep vein thrombosis in patients with bilaterally negative, unilaterally positive, and bilaterally positive after-exercise thermography

	Result of after-exercise thermography		
	Bilaterally negative	Unilaterally positive	Bilaterally positive
No (%) of patients	54(22.2)	22(18.2)	36(27.8)

As expected, the incidence of thrombosis as detected by the fibrinogen-uptake test was higher in the patients who had undergone hip surgery than in the group given abdominal operations (33.8 % and 8.8 %). There was no significant difference in mean age (67.8 and 67.2 years) or sex ratio between patients who had had positive and negative thermograms. The type of thrombosis prophylaxis and type of operation did not significantly influence the incidence of thrombosis in relation to the result of after-exercise thermography (table IV).

Table IV-Incidence of thrombosis as detected by fibrinogen-uptake test in relation to result of after-exercise thermography, type of thrombosis prophylaxis, and operation. Results expressed as number (%) of patients

	Results of after-exercise thermography	
	Positive	Negative
Prophylaxis:		
Dextran	4/25(16)	5/28(18)
Dextran + dihydro-ergotamin	10/33(30)	7/26(27)
Type of operation:		
Abdominal	3/24(13)	1/23(4)
Hip	11/34(32)	11/31(35)

Discussion

Deep vein thrombosis is one of the commonest and most important complications of surgery. Hence much effort has been aimed at finding a test that will detect patients at high risk. Most of this work has been directed towards disclosing changes in the coagulatory system. The techniques, however, are complex and expensive and therefore unsuited to routine practice. In 1978 Henderson et al² reported that a characteristic pattern in thermograms made after exercise could help to predict the risk of postoperative thrombosis. Using the fibrinogen-uptake test they found thrombosis after abdominal surgery in 11 % of patients who had had bilaterally negative thermograms, 63 % of those who had had unilaterally positive thermograms, and 92 % of patients who had had bilaterally positive thermograms. After elective hip operations the corresponding figures were 30 %, 56 %, 75 %. Statistically the results were highly significant.

We failed to reproduce these results, though our criterion for a positive thermogram was that used by Henderson

et al.². The pattern in a positive thermogram is characteristic, but there are borderline cases in which interpretation is difficult, especially if the patient has varicose veins. The true nature of the changes causing the characteristic pattern is still obscure. In another study (unpublished observations) our group was unable to correlate the pattern with deep venous insufficiency as measured from ambulatory venous pressure or by plethysmography.

The patients in our series were somewhat different from those described by Henderson et al.². Our patients were older. Also they had received prophylaxis against postoperative thrombosis. Though this prophylaxis may have influenced the results, it seems improbable that the thromboses so prevented were those that might be predicted by after-exercise thermography.

In conclusion, we were unable to show that a positive after-exercise thermogram is of value for predicting postoperative thrombosis as detected by the fibrinogen-uptake test.

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After-exercise thermography compared to strain-gauge plethysmography and venous pressure measurements to detect deep venous insufficiency

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After-exercise thermography (AET) has been claimed to be a means of detecting deep venous insufficiency. The question was studied in 167 patients four to five years after major surgery. The tests at follow-up included AET, strain-gauge plethysmography and venous pressure measurements in addition to clinical examination and a questionnaire concerning history, symptoms etc. No correlation was found between abnormal AET and objective manifestations of deep venous insufficiency.

Key-words: strain-gauge plethysmography; thermography; venous insufficiency; venous pressure

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The technique of after-exercise thermography (AET) was described by Cooke & Pilcher [1] and by Henderson *et al.* [4]. They claimed that an abnormal AET indicated a defective calf muscle pump and thus deep venous insufficiency. The available literature contains no reports in which AET was evaluated against objective methods of diagnosing deep venous insufficiency. We have earlier reported that AET cannot be used to predict postoperative thrombosis [7]. This study was designed to further investigate the diagnostic usefulness of AET in deep venous insufficiency assessed both clinically and with venous pressure and plethysmographic measurements.

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MATERIAL

167 patients were studied four years or more (mean 56.5 months) after major surgery. Mean age of patients was 70.5 years. Hip replacement surgery had been performed in 85 patients and abdominal surgery in 82.

METHODS

The patients case records were reviewed and the patients answered a questionnaire concerning symptoms that could indicate venous insufficiency. Symptoms asked for were leg ulcer, swollen legs, eczema of the leg, nocturnal cramps,

varicose veins and the need for constant pressure bandaging or elastic stocking.

In all patients the clinical status of the leg was recorded (leg ulcer, venous eczema, discolouration, swollen leg and varicose veins). AET, strain-gauge plethysmography and venous pressure recordings were performed. For AET the AGA 680 Medical System was used. A grey tone thermogram was taken when the patient had rested for at least 10 min with legs undressed. Room temperature was 21°C. During registration the patient was supine with legs raised more than 15°. Thereafter the patient exercised by walking on the spot for 3 min and a second thermogram was immediately recorded in the same position as before. When the second, but not the first, thermogram showed a network of linear hot spots crossing the anterior tibia the result was regarded as positive. The criteria for positive AET are the same as those set up by Henderson *et al.* [4]. Interpretation of the thermograms were done by one of us (B.L.) without foreknowledge of the results of the other tests.

Venous occlusion strain-gauge plethysmography was performed as described by Hallböök & Göthlin [3] and ambulatory plethysmography according to Holm [5]. A reserve venous volume (RVV) less than 1.5 ml/100 ml tissue, maximal venous emptying (MVE) less than 30 ml/100 ml tissue/min and a return time less than 8 sec were regarded as abnormal [3, 5]. Venous pressure was measured by inserting a scalp vein needle, connected to a pressure transducer, into a dorsal foot vein. An after-exercise pressure fall less than 30 mmHg and return time less than 25 sec were classified as pathologic [6].

RESULTS

Results are presented in Table I. The only difference between AET-positive and AET-negative legs concerning subjective manifestations of venous insufficiency was that AET-positive legs had more varicose veins and more commonly needed pressure bandaging. At the clinical examination no difference was seen between AET-positive and AET-negative legs, apart from greater frequency of varicose veins, particularly in the thigh, in the AET-positive legs. The results of plethysmography and venous pressure measurements showed no statistically significant differences between AET-positive and AET-negative legs. 'Clinical' venous insufficiency (leg ulcer during follow-up and/or two

TABLE I. 'Objective' venous insufficiency and AET (number of legs)

	Disease		Total
	Present	Absent	
AET			
Positive	28	100	128
Negative	40	166	206
Total	68	266	334

Prevalence 20%

Sensitivity 41%

Specificity 62%

Predicted value of a positive test = $28/128 = 22\%$ (15–30)*

Predicted value of a negative test = $166/206 = 81\%$ (74–85)*

* Approximate 95% confidence limits (Documenta Geigy: *Mathematics and Statistics*, p. 85: 'Exact' confidence limits for *P*).

or more subjective manifestations or clinical signs of venous insufficiency) was found in 41 legs. AET was positive in 19 (46.3%).

'Objective' venous insufficiency (pathologic return time at pressure recording and/or $MVE < 30$ ml/100 ml tissue/min) was found in 28% of AET-positive legs and 24% of AET-negative legs. Only 41% of the legs with 'objective' venous insufficiency are detected with AET.

DISCUSSION

In the present study no correlation was demonstrable between deep venous occlusion or valvular insufficiency and positive AET. The usefulness of our objective methods are well documented [2, 3, 6, 8, 9]. The difference between our results and those reported from Great Britain [1, 4] are difficult to explain. The thermographic technique, equipment and criteria for positive AET, as well as the patient groups, are obviously the same. It is obvious that some patients show a very distinct pattern on the thermogram after exercise but the causal factors of this characteristic pattern still remain obscure.

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Deep venous insufficiency after postoperative thrombosis diagnosed with ^{125}I -labelled fibrinogen uptake test

Postoperative thrombosis detected with the ^{125}I -labelled fibrinogen uptake test (FUT) is frequent. FUT correlates well with phlebography and a positive FUT is associated with high incidence of pulmonary embolism. This study has been performed to evaluate venous function 3-5 years after FUT-detected thrombosis. A follow-up examination was performed in 381 patients who had been studied after operation with FUT. The follow-up included a questionnaire, clinical examination, venous occlusion strain-gauge plethysmography, ambulatory strain-gauge plethysmography, venous pressure examination and, in some cases, Doppler ultrasound examination of venous valve function in the leg. No statistically significant differences were found in any parameters used between legs with and without FUT-detected postoperative thrombosis, except that more FUT-positive legs had an abnormal venous pressure decrease during exercise than FUT-negative legs. The frequency of deep venous insufficiency was equal in FUT-positive and FUT-negative legs. Moreover the frequency of deep venous insufficiency was not affected by the site of the FUT-detected thrombosis or by the different kinds of prophylactics used. The frequency of venous insufficiency was high.

Keywords: Venous insufficiency, venous thrombosis, fibrinogen uptake test, postoperative complications, thrombosis prophylaxis

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Postoperative deep vein thrombosis can be detected with the ^{125}I -labelled fibrinogen uptake test (FUT), a method which correlates well with phlebography. A positive test indicates a risk of developing pulmonary embolism, and it has been extensively used in screening investigations, especially thromboprophylactic methods. The incidence of thrombosis detected by the fibrinogen test is high after most types of surgery. One important problem which is not satisfactorily documented is whether a positive test reflects a risk of impairment of venous function.

The purpose of the present study was late evaluation of venous function of legs after FUT-detected postoperative thrombosis. The influence of different types of prophylaxis on the development of venous insufficiency was also analysed.

Material and methods

Material

Five hundred and five patients who had participated in three separate studies of prophylaxis against postoperative thromboembolism¹⁻³ were requested to attend a follow-up examination. Four hundred and forty-eight patients (88.7 per cent) responded and were examined. Of these patients, 67 had to be excluded because of incomplete FUT (43 patients) or some technical failure at follow-up. The patients excluded did not differ in age, sex, follow-up time, type of operation or frequency of positive FUT from the patients included. The study thus includes 381 patients (211 men and 170 women). Mean age at follow-up was 71.1 years (range 53-87 years) and the postoperative interval averaged 51.3 months (range 37-76 months). The operation had consisted of elective hip surgery in 211 patients and abdominal surgery in 170.

The 57 patients who could not be reached for a follow-up examination were somewhat older than the patients studied (mean age 77 years). The male/female ratio was the same. Somewhat fewer

had elective hip surgery (42 as compared to 55 per cent). The frequency of FUT-positive legs was 22 per cent (18 per cent in the group studied). The distribution between the different prophylaxis groups did not differ significantly from the patients studied. Twelve patients had died during the follow-up period.

Seventy-two patients were untreated controls; 102 had received dextran 70, 62 low-dose heparin, 80 low-dose heparin in combination with dihydroergotamine (DHEH) and 65 a heparin analogue, sodium pentosan polysulphate (Pz68).

FUT had been performed in all patients at the time of operation using the method described by Kakkar *et al.*⁴, slightly modified⁵. Measured activity was correlated with the precordial activity. An uptake increase of 20 per cent or more as compared to adjacent points on two consecutive measurements was accepted as the diagnostic criterion for deep venous thrombosis. FUT was bilaterally negative in 279 patients, bilaterally positive in 35 and unilaterally positive in 67 patients. Treatment for thrombosis was given to five patients with clinical evidence of thrombosis in the immediate postoperative period (1.3 per cent). Phlebography was not routinely performed postoperatively.

Seventeen patients (4.6 per cent) had been treated for deep venous thrombosis during the follow-up period. Of these 11 had been FUT-negative at the time of operation, 4 had a bilaterally positive FUT and 2 unilaterally positive FUT.

One hundred and thirty-three patients (35 per cent) had undergone further surgery during the follow-up period. None had a second FUT. These patients were equally distributed in the different groups analysed, i.e. according to age, sex, type of operation, type of prophylaxis and FUT result.

Methods

The patients answered a questionnaire concerning subjective manifestations of venous disorders of the leg during the follow-up period and their present state of health. All patients were clinically re-examined. The presence of varicose veins, crural eczema, discoloration, swelling and leg ulcers were recorded.

'Clinical' deep venous insufficiency was considered present when a patient had a leg ulcer after operation and/or at least two symptoms or signs of venous insufficiency (swelling or discoloration of the leg, crural eczema or need for pressure bandage or com-

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Table 1 Subjective manifestations of venous insufficiency (replies of questionnaire)

	FUT-negative legs		FUT-positive legs		Statistical significance
	No.	%	No.	%	
Total number	625		137		
Symptoms during follow-up period					
Leg ulcer	19	3.0	5	3.6	n.s.
Swollen leg	133	21.3	26	18.8	n.s.
Varicose veins	74	11.9	20	14.5	n.s.
Discolouration of leg	56	9.0	19	13.7	n.s.
Crural eczema	58	9.3	13	9.4	n.s.
Nocturnal cramps	142	22.8	22	15.9	n.s.
Pressure bandage or compression stockings constantly required	21	3.4	7	5.1	n.s.

pression stockings). Venous occlusion strain-gauge plethysmography was performed according to the method described by Hallböök *et al.*⁶⁷. The parameters used in the evaluation were reserve venous volume (RVV) in ml/100 ml tissue and maximum venous emptying (MVE) in ml/100 ml tissue and minute. An RVV of less than 1.5 and an MVE of less than 30 were classified as pathological. Ambulatory venous strain-gauge plethysmography was performed according to Holm^{8,9}. Return time less than 8 s was regarded as pathological.

Ambulatory venous pressure measurements were performed in 674 legs. A dorsal vein of the foot was percutaneously catheterized with a scalp-vein needle and connected to a pressure transducer. The pressure fall and return time (from termination of exercise to restitution of pre-exercise pressure) were registered. The superficial veins were occluded during measurements with a rubber tourniquet with slight pressure in order to avoid superficial venous insufficiency to interfere with the results. A pressure fall of less than 30 mmHg and return time of less than 25 s were regarded as abnormal¹⁰⁻¹².

In 394 legs the presence of venous valve insufficiency was recorded with Doppler ultrasound technique in the femoral and popliteal vein¹³.

The arterial ankle/arm pressure index was measured with Doppler ultrasound technique to evaluate the arterial circulation.

The patients had not been informed of the FUT results before follow-up examination and the interpretation of data obtained was made without knowledge of the FUT results.

For statistical calculations the χ^2 method was used.

Table 3 Results of venous-occlusion plethysmography, venous pressure and Doppler-examinations

	FUT-negative legs		FUT-positive legs		Statistical significance
	No.	%	No.	%	
Venous occlusion plethysmography					
Total studied	620		135		
RVV < 1.5 ml/100 ml tissue	63	10.2	9	6.6	n.s.
MVE < 30 ml/100 ml tissue per min	72	11.6	21	15.5	n.s.
Ambulatory plethysmography					
Total studied	471		84		
Return time < 8 s	262	42.0	42	50.0	n.s.
Venous pressure					
Total studied	566		108		
Pressure decrease < 30 mmHg	49	8.6	19	17.6	0.05 > P > 0.01
Return time < 25 s	111	19.6	31	28.7	n.s.
Doppler measurements					
Total studied	361		33		
Insufficiency femoral vein	74	20.5	12	36.4	n.s.
Insufficiency popliteal vein	67	18.6	8	24.2	n.s.
'Objective' venous insufficiency	159	25.4	45	28.9	n.s.

Table 2 Findings at clinical examination

	FUT-negative legs		FUT-positive legs		Statistical significance
	No.	%	No.	%	
Total number	625		137		
Clinical findings					
Edema	97	15.5	27	19.5	n.s.
Crural eczema	98	15.7	20	14.5	n.s.
Discolouration	161	25.8	37	26.8	n.s.
Leg ulcer	7	1.1	3	2.2	n.s.
Varicose veins of leg	260	41.7	54	39.1	n.s.
Varicose veins of thigh	105	16.8	19	13.8	n.s.
'Clinical' deep venous insufficiency	135	21.6	31	22.4	n.s.

Results

Results were recorded for each leg separately. Six hundred and twenty-five legs were FUT-negative (82 per cent) while 137 were FUT-positive (18 per cent). Of the legs with a positive FUT, 99 (72.3 per cent) had the fibrinogen uptake strictly located below knee while 38 (27.7 per cent) were located above knee. In patients operated upon with elective hip surgery 99 legs (23.5 per cent) showed a positive FUT while in the abdominal surgery group 38 legs (11.2 per cent) were FUT-positive.

In Table 2 the results of the follow-up questionnaire are presented. There were no statistically significant differences between legs with a positive FUT postoperatively and patients with a negative FUT. Nor did the clinical examination reveal any statistically significant changes between FUT-positive and FUT-negative legs (Table 2).

Table 3 shows the results of plethysmography, venous pressure recordings and Doppler measurements at follow-up. The only statistically significant difference is that more FUT-positive legs showed an abnormal pressure decrease during exercise than FUT-negative legs. The number of FUT-positive legs that have been examined with Doppler for detection of venous valve insufficiency was small and thus the results of this test are difficult to evaluate. However, there was no difference between FUT-positive and FUT-negative legs when impaired MVE or abnormally fast

Table 4 Results according to location of FUT-detected thrombosis

	FUT-positive legs					
	Total		Below knee only		Above knee	
	No.	%	No.	%	No.	%
Total	137		99		38	
'Clinical' insufficiency	31	22.4	24	24.2	7	18.4
Venous occlusion plethysmography	135		97		38	
RVV < 1.5	9	6.6	7	7.2	2	5.3
MVE < 30	21	15.5	16	16.5	5	13.1
Ambulatory plethysmography	84		64		20	
Return time < 8	42	50.0	32	50.0	10	50.0
Venous pressure	108		83		25	
Pressure decrease < 30	19	17.6	14	16.7	5	20.0
Return time < 25	31	28.7	26	31.3	5	20.0
Doppler examination	33		25		8	
Insufficiency femoral vein	12	36.4	7	28.0	5	62.5
Insufficiency popliteal vein	8	24.2	8	40.0	0	—
'Objective' insufficiency	45	28.9	37	37.4	8	21.0

pressure return after exercise indicating venous obstruction and venous valve insufficiency respectively are considered separately or in combination ('objective' venous insufficiency).

In Table 4 results between legs with a positive FUT below knee and above knee are compared. The number of pathological findings in the respective groups is small. The differences between the groups are not statistically significant.

Results at follow-up in the different prophylaxis groups are recorded in Table 5. While the results of FUT differed a great deal between the groups there were no statistically significant changes between the groups at follow-up with respect to 'clinical' and 'objective' venous insufficiency.

Table 5 Results according to type of prophylaxis (number of legs)

	Controls		Dextran 70		Low-dose heparin		DHEH		Pz 68	
	No.	%	No.	%	No.	%	No.	%	No.	%
No. in groups	144		204		124		160		130	
FUT										
Positive (total)	43	29.9	58	28.9	23	18.6	8	5.0	6	4.6
Positive below knee only	34	23.6	39	19.1	15	12.0	6	3.8	6	4.6
Positive above knee	9	6.2	19	9.3	8	6.4	2	1.2	0	—
'Clinical' insufficiency	26	18.1	45	22.1	18	14.5	35	21.9	42	32.3
Venous occlusion plethysmography	142		202		124		158		130	
RVV < 1.5	9	6.3	17	8.4	10	8.0	17	10.8	19	14.6
MVE < 30	18	12.7	22	10.9	13	10.5	18	11.4	22	16.9
Ambulatory plethysmography	53		150		86		142		128	
Return time < 8	17	32.0	78	52.0	37	43.0	85	59.9	87	68.0
Venous pressure	118		180		109		146		115	
Pressure decrease < 30	25	21.2	19	10.6	16	14.7	2	1.4	6	5.2
Return time < 25	29	24.6	33	18.3	19	17.4	29	19.9	32	27.8
'Objective' insufficiency	42	29.2	50	24.5	26	21.0	42	26.3	44	33.8

In the hip surgery group 127 legs (30.1 per cent) showed 'clinical' insufficiency at follow-up compared with 39 (11.5 per cent) in the abdominal surgery group ($P < 0.001$). The figures for 'objective' insufficiency were 141 (33.4 per cent) and 63 (18.5 per cent) respectively ($P < 0.001$).

In the 67 patients with a unilateral positive FUT where all parameters are alike, except the difference between the FUT-positive and FUT-negative leg, the frequencies of 'clinical' and 'objective' insufficiency were 31.3 per cent and 29.8 per cent respectively in the FUT-positive legs compared with 31.3 per cent and 35.8 per cent in the FUT-negative legs.

One hundred and thirty-three patients (35 per cent) underwent further surgery during the follow-up period. In these patients 65 (24.4 per cent) of the legs showed 'clinical' insufficiency and 67 legs (25.2 per cent) showed 'objective' insufficiency at follow-up compared with the total material where the figures for 'clinical' and 'objective' insufficiency were 21.8 per cent and 26.9 per cent respectively.

Thirty-three patients (8.7 per cent) gave a history of thrombosis before the FUT investigation. In all cases this thrombosis had been unilateral. Six of these patients (18.2 per cent) had a positive FUT and three (9.1 per cent) had a bilaterally positive FUT. This should be compared with the total material where the frequency of positive FUT and bilaterally positive FUT was 26.7 and 9.2 per cent respectively.

At follow-up 15 of the 33 legs with previous thrombosis (45.4 per cent) had 'clinical' insufficiency compared with 20.7 per cent in the rest of the material (legs with previous thrombosis excluded) ($P < 0.01$). The figures for 'objective' insufficiency were 42.4 per cent (14 legs) and 26 per cent respectively (n.s.).

If the legs with previous thrombosis are excluded from the total material (Table 6) the results are not significantly changed.

When the patients were analysed according to age group (Table 7) the frequency of positive FUT was not significantly different in the different groups. The ratio between hip surgery and abdominal surgery was also the same in the different groups. When the 'clinical' insufficiency is recorded there are no statistically significant differences between the groups although there is a tendency towards more insufficiency in the higher age groups. 'Objective' insufficiency was recorded significantly less often in patients less than 60 years than in higher age groups ($P < 0.01$).

The arterial ankle/arm pressure was measured in all patients. An index of less than 0.95 was found in 31.3 of

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Table 6 Results at follow-up when legs with previous thrombosis have been excluded

	FUT-negative legs		FUT-positive legs		Statistical significance
	No.	%	No.	%	
Total	598		131		
'Clinical' insufficiency	124	20.7	27	20.6	n.s.
Venous occlusion plethysmography					
Total studied	593		131		
RVV < 1.5 ml/100 ml tissue	61	10.3	8	6.1	n.s.
MVE < 30 ml/100 ml tissue per min	67	11.3	19	14.5	n.s.
Ambulatory plethysmography					
Total studied	464		83		
Return time < 8 s	246	53.0	41	49.4	n.s.
Venous pressure					
Total studied	561		107		
Pressure decrease < 30 mmHg	42	7.4	18	16.8	0.01 > P > 0.001
Return time < 25 s	102	18.2	27	25.2	n.s.
Doppler measurements					
Total studied	349		27		
Insufficiency femoral vein	71	20.3	12	44.4	
Insufficiency popliteal vein	61	17.4	8	29.6	
'Objective' insufficiency	148	24.7	42	32.0	n.s.

FUT-positive legs and in 36.7 per cent of FUT-negative legs. No patient had an index of less than 0.7.

Discussion

The fibrinogen uptake test is a well established method for detecting postoperative thrombosis. FUT shows good correlation with plebography^{14,15} and a positive FUT indicates a risk for postoperative pulmonary embolism^{16,17}. The sensitivity is high¹⁸ but since FUT detects very small thrombi the clinical relevance of a FUT-detected thrombosis has been debated.

Deep venous insufficiency (DVI) after deep vein thrombosis is a well-known entity. The frequency of DVI after phlebographically proven thromboses varies between 25 per cent to 72 per cent in the literature¹⁹⁻²¹. The frequency of DVI seems to increase with time after the thrombosis. DVI developing without previous known thrombosis has also been reported and the frequency varies from 7 to 30 per cent²⁰⁻²². The frequency of DVI after FUT-detected thrombosis is however less well-known. In an earlier series of 179 patients we have reported a frequency of DVI of about 25 per cent four to five years after operation irrespectively of positive or negative FUT at the time of operation²³. Three other follow-up studies of postoperative DVI after FUT-detected thrombosis have been reported where the diagnosis of DVI was based only on clinical examination^{22,24,25}. In

these studies the frequency of DVI varied between 3 and 11 per cent. In a study with venous occlusion strain-gauge plethysmography 3 years after FUT-detected thrombosis, 5 of 50 patients revealed pathological plethysmograms²⁶.

The present study showed no significant differences in DVI between legs with and without FUT-detected thrombosis as observed clinically or with different objective methods. The only difference that was noted was that more FUT-positive legs showed an abnormal pressure decrease during exercise than FUT-negative legs. The mean pressure decrease of FUT-positive and FUT-negative legs was however not significantly different (46.2 mmHg and 54.1 mmHg respectively). The total number of legs with a pathological pressure decrease is however small and the significance of this is doubtful. The length of the follow-up period is well in accordance with other studies of post-thrombotic syndromes^{21,24,27} and should be adequate for reliable results.

The methods used for objective screening of DVI (venous occlusion strain-gauge plethysmography, ambulatory strain-gauge plethysmography, venous pressure recordings and Doppler ultrasound) are well established and documented^{6-13,28}.

The fact that so many FUT-negative legs developed DVI is interesting. The results are however well in accordance to the figures reported by Kistner²⁹. He suggests that as much as 50 per cent of DVI is sequela not to post-thrombotic destruction of venous valves, but to venous valves that weaken with age and start to leak. The high frequency of DVI in FUT-negative legs in this series could be explained that way. The patients in the present series are also quite old.

Further surgery during the follow-up period did not affect the results. A higher incidence of DVI might have been expected since there is a known risk of recurrence of thrombosis. However the results are compatible with the lack of significant difference between FUT-positive and FUT-negative legs.

The extent of the FUT-detected thrombosis did not affect the results. Both thrombosis located strictly below knee level and thrombosis above knee showed the same frequency of DVI at follow-up. The number of thromboses above knee level is however small and further studies are required for

Table 7 Results according to age-group (number of legs)

	50-59		60-69		70-79		≥ 80	
	No.	%	No.	%	No.	%	No.	%
Total	56		344		306		56	
FUT-positive	10	17.8	58	16.8	63	20.5	6	10.7
Hip surgery	24	42.8	184	53.5	182	59.4	32	57.2
'Clinical' insufficiency	11	19.6	62	18.0	77	25.1	17	30.3
'Objective' insufficiency	5	8.9	90	26.1	94	30.7	15	26.8

confirmation of this finding. Some patients had had a thrombosis before the FUT investigation. This did not influence the frequency of FUT-detected postoperative thrombosis although these patients might have been expected to have a higher risk of developing thrombosis.

The type of prophylaxis against postoperative thrombo-embolism did not influence the frequency of DVI at follow-up (Table 5). Both 'clinical' and 'objective' DVI was as common in the different prophylaxis groups as in the control group. These findings suggest that prophylaxis against postoperative thrombo-embolism does not prevent the development of DVI even if the number of FUT-detected thromboses can be reduced. Other factors may be more important in the development of DVI so that the effect of prophylaxis on FUT-detected thrombosis can not be registered. However it is important that prophylaxis does reduce pulmonary embolism, both lethal and non-lethal, and is therefore indicated^{3,30-32}.

In conclusion this study shows that, after an observation period of 3-5 years after operation, no significant differences as regards the frequency of deep venous insufficiency could be found between legs with and without FUT-detected thrombosis at the time of operation. The level of the FUT-detected thrombosis did not influence the results. Although the frequency of FUT-detected thromboses varied between the different thromboprophylaxis groups, the frequency of deep venous insufficiency at follow-up was the same in the different groups.

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VENOUS FUNCTION FIVE TO EIGHT YEARS AFTER CLINICALLY
SUSPECTED DEEP VENOUS THROMBOSIS

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ABSTRACT

One hundred and fifty-four patients, who had been subjected to phlebography 5-8 years previously because of clinical suspicion of deep venous thrombosis (DVT), were investigated to evaluate the frequency of deep venous insufficiency (DVI). The evaluation included clinical examination, registration of subjective complaints and objective measurements with plethysmography, venous pressure and Doppler ultrasound. DVT had been present in 75 legs. There were no statistically significant differences between legs with and without earlier DVT apart from more venous outflow obstruction in the former. DVI was as common after calf vein thrombosis as after more proximal DVT. DVI was more frequent in elderly patients and in patients with at history of previous DVI or DVT. The sufficiency of the popliteal vein seemed to be of great importance in the development of DVI. More than one third of legs without DVT had developed DVI at follow-up.

Key words: thrombophlebitis, venous insufficiency, phlebography.

INTRODUCTION

Deep venous insufficiency (DVI) is known to be a result of deep venous thrombosis (DVT) but in later years other factors predisposing to DVI have been discussed. There has been disagreement about what the anatomical extension of DVT means for the development of DVI. It is not known whether it is possible from the acute phlebographic pattern to predict which patients will develop DVI.

The purpose of the present study therefore was to evaluate the late venous function of legs in patients who previously had had clinical suspicion of deep venous thrombosis and where phlebography was performed. This leaves us with three groups of legs to compare: legs in which an earlier phlebography had shown DVT, legs in which an earlier phlebography had shown normal conditions and legs in which phlebography not had been performed.

MATERIAL

During the years 1976 - 1977 223 patients were examined in our hospital with phlebography because of clinically suspected DVT. Twentynine patients had died during the follow-up period. The remaining 194 patients (122 female) were requested to attend a follow-up examination. 154 patients (83 female) responded and were examined. The investigated patients were younger (61.3 (25 - 89) years) than the dropouts (69.8 (42 - 88) years) and dead (73.4 (40 - 93) years). Follow-up time, number of DVT's and extent of DVT did not differ between the investigated patients and the drop-outs.

A total of 160 phlebographies were performed in the 154 investigated patients. Six patients had had a bilateral phlebography. 75 DVT's were found (46.9%) in 74 patients. The mean age of the patients with and without DVT was the same. The thrombosis was leftsided in 32 patients,

rightsided in 41 patients and bilateral in one. The extent of DVT's is given in Table I.

Anticoagulant treatment for thrombosis had been given to all patients with thrombosis except three with small calf-vein thrombi, who were treated with compression bandage only. Three legs with negative phlebography were treated (bilateral phlebography with unilateral DVT).

Table I

Extension of DVT

	Calf veins	Popliteal vein	Distal femoral vein	Proximal iliac femoral vein	
No of DVT					
39	X				
1		X			
4	X	X			
3	X		X		
11	X	X	X		
2		X	X		
6	X	X	X	X	
3		X	X	X	
1			X	X	
2		X	X	X	X
2	X		X	X	X
1		X			X

Ten patients with negative phlebography (12.5%) and 16 patients with positive phlebography (21.6%) gave a history of earlier DVT. Symptoms of DVT prior to the phlebography was given by 18 patients with negative phlebography (22.5%) and 18 patients with DVT (24.3%). Earlier DVT was looked for in the patient file and also asked for

in the questionnaire. We tried to omit earlier superficial thrombophlebitis. Earlier DVI was asked for in the questionnaire, where earlier leg ulcer, swolleness, crural eczema and nightly cramps were registered.

METHODS

Phlebography was performed according to the technique advocated by Greitz (1) and Rabinov and Paulin (2) and evalutated by senior radiologists.

At follow-up the patients answered a questionnaire concerning symptoms of venous disorders of the legs during the follow-up period and their present state of health. All patients were clinically examined for signs of venous disorders. Presence of varicose veins, crural eczema, discoloration, swelling and leg ulcers were looked for.

"Clinical" deep venous insufficiency was considered present when a patient had had leg ulcer during the follow-up period and/or at least two symptoms or signs of venous insufficiency (swelling, discoloration, crural eczema or need for pressure bandage or compression stockings).

Venous occlusion strain-gauge plethysmography was performed according to the method described by Hallböök et al (3,4). The parameters used in the evaluation were reserve venous volume (RVV) in ml/100 ml tissue and maximum venous emptying (MVE) in ml/100 ml tissue and minute. RVV less than 1.5 and MVE less than 30 were classified as pathologic (3,4).

Ambulatory venous pressure measurements were performed. A dorsal foot vein was percutaneously catheterized with a scalp-vein needle and connected to a pressure transducer.

The pressure fall and return time (from termination of exercise to restitution of preexercise pressure) were

registered. The superficial veins were occluded during measurements with a rubber tourniquet with slight pressure in order to avoid superficial venous insufficiency to interfere with the results. A pressure fall of less than 30 mmHg and return time of less than 25 seconds were regarded as abnormal (5,6,7).

Venous valve insufficiency was also recorded with doppler ultrasound technique in the femoral and popliteal vein as described by Barnes (8).

"Objective" venous insufficiency was considered present when plethysmography showed impaired outflow ($MVE < 30$) and/or venous pressure measurements showed valvular insufficiency (return time < 25) and/or doppler showed insufficiency in the femoral or popliteal vein.

The arterial ankle/arm pressure index was measured with doppler ultrasound technique to evaluate the arterial circulation. An index of more than 0.95 was regarded normal.

For statistical calculations the chi-square method and Student's t-test were used. Significance was considered when $p < 0.05$.

RESULTS

Results were recorded for each leg separately. 75 legs had a phlebographically proven DVT, 85 legs a normal phlebography and 148 legs were not examined with phlebography.

The results of the questionnaire and the clinical examination at follow-up showed only one significant difference. "Clinical" deep venous insufficiency was more common in legs with normal phlebography (51 %) than in legs not subject to phlebography (34 %; $p < 0.05$). There was no

Table II

Results of plethysmography, venous pressure and doppler examinations.

	Plebographically proven DVT		Plebographically no DVT		No phlebography	
	No	%	No	%	No	%
<u>Plethysmography</u>						
Total studied	74		85		148	
RVV <1.5 ml/100 ml tissue	6	8.1	5	5.9	16	10.8
MVE <30 ml/100 ml tissue/min	14	18.9	6	7.1	16	10.8
<u>Venous pressure</u>						
Total studied	71		77		139	
Pressure decrease <30 mm Hg	5	7.0	0		6	4.3
Return time <25 sec	22	31.0	22	28.5	27	19.4
<u>Doppler</u>						
Total studied	71		81		141	
Insufficiency femoral vein	11	15.5	14	17.3	15	10.6
Insufficiency popliteal vein	15	21.1	7	8.6	11	7.8
"Objective" deep venous insufficiency	37	49.3	35	41.2	47	31.8

X = $p < 0.05$

difference though between legs with phlebographically proven DVT (44 %) and phlebographically normal legs.

Results of objective tests for DVI are presented in Table II. Significantly more legs with proven DVT had a venous outflow obstruction ($MVE < 30$), less pressure decrease at exercise and more insufficiency in the popliteal vein valves than legs with normal phlebography. Moreover insufficiency of the popliteal vein and "objective" venous insufficiency was significantly more common in legs with DVT than in legs that had not been subject to phlebography. No significant differences were noted between legs with normal phlebography and unphlebographed legs. "Clinical" and "objective" deep venous insufficiency was present in 28.0 % of legs not subject to phlebography.

An analysis was made of legs with DVT strictly located below knee level (39 legs) and legs with DVT extending into or above the popliteal vein (36 legs). The only statistically significant difference was that legs with more extensive DVT more often had outflow obstruction ($MVE < 30$) at follow-up (31 % vs 8 %; $p < 0.05$).

"Objective" venous insufficiency was significantly more common in patients over 65 years than in those below (63 % vs 30 %; $p < 0.05$). "Clinical" insufficiency did not differ according to age but the older patients had more often a history of earlier DVI (34 % vs 13 %; $p < 0.05$).

The phlebographic extension of thrombosis did not differ in patients above and below 65 years.

In legs without phlebographically proven DVT there were no statistically significant differences between patients below and above 65 years. Looking at all legs (regardless of DVT or not) "objective" insufficiency was significantly more common in the older age groups (55.7 % vs 32.2 %; $p < 0.05$) while "clinical" insufficiency did not differ.

The development of DVI was not influenced by sex and was as common in right and left legs.

An ankle/arm arterial pressure index <0.95 was present in 100 legs in 64 patients. In these legs "objective" venous insufficiency was present in 60 legs (60 %) as compared to 57 of the 208 legs with normal arterial circulation (27.4 %; $p<0.01$). "Clinical" venous insufficiency was present in 55 legs with index <0.95 (55 %) as compared to 71 legs with normal index (34.1 %; $p<0.001$).

Mean age of patients with impaired arterial circulation was significantly higher than in those with normal arterial index (63.5 vs 57.8 years; $p<0.05$). In patients under 65 years "clinical" and "objective" venous insufficiency was as common in legs with arterial index <0.95 as in legs with index >0.95 and the same was true for patients over 65 years. The frequency of both "clinical" and "objective" venous insufficiency was significantly more common in patients over 65 years both in legs with normal and impaired arterial circulation.

In the 32 patients with a history of earlier DVI significantly more legs had clinical insufficiency (72%) than patients without earlier DVI (33.4% ($p<0.001$)). The figures for "objective" insufficiency in these groups were 54.7 % and 33.6 % respectively ($p<0.05$). Mean age of these patients did not differ significantly from the mean age of patients without history of earlier DVI.

In patients with history of earlier thromboembolic disease (24 patients) there was also higher frequency of legs with "clinical" venous insufficiency than in patients without (60.4% and 37.3% respectively, $p<0.05$). "Objective" venous insufficiency was also more common in patients with earlier thromboembolic disease, 64.6 % as compared to 33.0% in patients without ($p<0.001$). The mean age did

not differ in patients with and without history of earlier thromboembolic disease.

In Table III legs with and without reflux in the popliteal vein as measured by doppler are compared. It can be seen that both "clinical" insufficiency and abnormal MVE and/or return time are significantly more common in legs with insufficiency in the popliteal valve than legs without.

When comparing the frequency of DVI in legs with normal phlebography to the normal legs in patients with unilateral DVT no statistically significant difference was found. Also no difference in development of DVI could be found between legs with known DVT and their contralateral legs. Thus DVT in one leg does not seem to influence the development of DVI in the contralateral leg.

Table III

Results in legs with and without valvular reflux in popliteal vein.

	Reflux popliteal vein		No reflux popliteal vein		Statistical significance
	No	%	No	%	
Total	34		258		
♀	17	50.0	142	55.0	n.s.
DVT	15	44.1	55	21.3	p<0.01
"Clinical" insuff.	23	67.6	92	35.7	p<0.01
MVE <30	4	11.8	22	8.5	n.s.
Return time <25	20	58.8	48	19.1	p<0.001
MVE <30 and/or return time <25	21	61.7	66	25.6	p<0.001

DISCUSSION

The development of deep venous insufficiency after deep venous thrombosis is a well known and clinically important complication. Gjörres (9) estimated the minimum prevalence among adults in Sweden to be 1.8 %.

Access to new possibilities for non-invasive tests for DVI and the development of venous valve reconstructive surgery have somewhat changed the concept of the development of DVI.

So far most studies on development of DVI have not included a control group without thrombosis and thus the incidence of DVI in nonthrombotic legs is virtually unknown.

The frequency of DVT in this study is about 50 % which is well in accordance with other studies where patients have been subjected to phlebography on clinical suspicion of DVT.

The follow-up time in the present study should be adequate for reliable results as regards development of DVI (10,11,12). The results show that "clinical" DVI is not significantly different between legs with proven DVI phlebographically and legs without DVT but it is significantly less common in legs not subject to phlebography. This might be explained by the fact that phlebography was made on clinical suspicion of DVT and therefore the legs where no DVT was found could have had some condition which influenced the development of DVI.

Obstruction of the deep veins as demonstrated with plethysmography was significantly more common in legs with DVT than in legs without. Insufficiency of the venous valves was, however, not significantly different in legs with DVT and legs without DVT.

Plethysmographic obstruction of the deep veins was more common if the DVT had extended above knee level, but insufficiency of the venous valves were not, nor was "clinical" venous insufficiency. These findings correlate well with the results of Browse et al. (13).

Age seems to be an important factor in the development of DVI (17). In this study "objective" venous insufficiency was more common above the age of 65 than in younger persons. In patients without known DVT no corresponding difference could be found. This finding is contradictory to the findings of Browse et al (13). They could not find that age influenced the development of DVI.

The significance of a competent popliteal valve in the development of DVI could be clearly shown. Both "clinical" and "objective" venous insufficiency was highly significantly more common in patients with reflux in the popliteal vein as demonstrated by doppler ultrasound than in patients without. This is well in accordance with the results of Shull et al (10) and Partsch et al (15).

41 % of legs without known DVT developed some objective sign of DVI while the corresponding figure for legs with known DVT was 49 %. Thus a previous DVT is only one factor that predisposes to the development of DVI. Other unknown factors influence the deep veins. Aging of the venous valves may be one (16) but also undetected small thrombi might influence the development of DVI. Further studies are required.

Nearly all patients with DVT were treated with anticoagulants, why it is impossible to draw any conclusions on the effect of treatment on the development of DVI. Two possible explanations exist that DVI is equally frequent in nonthrombotic as thrombotic legs: Treatment does not influence the development of DVI, or treatment has an effect so that legs that might have developed DVI becomes

comparable to legs without DVT. To answer this question a long term prospective study comparing treatment versus no treatment of DVT would have to be performed.

Suggestions have been made that phlebography can induce DVT (17). In this study "clinical" insufficiency was more common in phlebographed legs without DVT than in unphlebographed legs, but there were no objectively measured differences. This might be explained by the fact that the phlebographed legs without DVT were not symptomless at the time of phlebography and thus might have had some condition predisposing to subjective manifestations of DVI.

The DVT's in this study were all clinically suspected. Is the frequency of DVI different after clinically silent DVT? In an earlier report from our group (14) we have studied late sequelae of postoperative DVT diagnosed with 125 I-fibrinogen uptake test (FUT), where almost all calf thrombi were clinically silent. The frequency of "clinical" venous insufficiency of calf vein DVT was in the FUT-group 24 % as compared to 41 % in the present study and objectively measured DVI was in the FUT-group 37 % as compared to 43.6 in this study. Thus it seems that at least objectively measured DVI does not differ between legs with clinically suspected and clinically silent calf vein thrombosis.

There are no earlier reports on the influence of arterial circulation on the development of DVI. In this study we found a significantly higher frequency of objectively measured DVI in patients with impaired arterial circulation than in normal subjects in spite of the fact that DVT was equally distributed in the groups. However, the patients with impaired arterial circulation was significantly older than the patients with normal arterial circulation, and within the age groups no difference in "objective" venous insufficiency could be demonstrated

between legs with normal and impaired arterial circulation. Thus we could not show any influence of arterial circulation on the development of DVI.

We conclude:

there are only minor differences in the development of DVI between legs with calf vein thrombosis as compared to legs with more proximal DVI,

about 1/3 of legs without previous known thrombosis develop DVI,

high age, history of earlier DVI or thromboembolic disease seem to be important factors in the development of DVI,

insufficiency of the popliteal vein is of great importance in the development of DVI.

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VENOUS FUNCTION AFTER FRACTURE OF THE LOWER EXTREMITY
A follow-up study eight to ten years after injury

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Key words

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malleolar fracture

Abstract

150 patients were examined eight to ten years after a fracture of the lower limb to evaluate whether the frequency of deep venous insufficiency (DVI) was influenced by the type of fracture. The evaluation included clinical examination, registration of subjective complaints, venous pressure measurements, measurements with plethysmography and doppler ultrasound. Symptoms and signs of DVI were more common in the fractured limbs than in the uninjured ones, while objectively diagnosed DVI did not differ between the groups. Only minor differences were present in the development of DVI between limbs with various types of fracture (hip fractures were not included in the study). High age and incompetence of the popliteal valves were more important in the development of DVI than the earlier fracture. The frequency of

objectively measured DVI in the fractured limbs was 35 per cent and in the uninjured limbs 30 per cent.

Introduction

Damage to the deep veins and development of deep venous thrombosis (DVT) after fractures of the lower limb is well known and documented (Bauer 1944, Jacob 1944, Sevitt & Gallagher 1959, Hjelmstedt & Sundström 1963, Hjelmstedt & Bergvall 1968, Culver et al 1970, Nylander & Semb 1972, Miehle 1982). What this means for the development of deep venous insufficiency (DVI) in the long run, however, is poorly understood and reports on this subject are scarce.

The purpose of the present study was to evaluate the venous function of legs in patients who previously had had a fracture of the lower extremity and to compare these legs with the contralateral legs without fracture and also to analyze whether the type and localization of the fracture influenced the development of DVI.

Patients and methods

During 1973-74 360 patients over 15 years of age were admitted to our hospital for fractures of the lower extremity. Fractures of the femoral neck, fractures of patella, multiple fractures and bilateral fractures were not included in the study. During the follow-up period, 129 patients had died or moved from the area and could not be investigated. The remaining 231 patients were asked to attend a follow-up examination. 150 patients responded and were investigated. Among the 81 patients who did not want to participate the mean age, types of fracture and sex distribution was the same as in those included in the study. Fiftyeight of the 150 investigated patients were women.

Table 1

Material according to type of fracture

	Type of fracture			
	Femoral	Condylar	Lower leg	Malleolar
Total number	26	8	53	63
Mean age at injury (years) and range	28.4 (15-72)	34.2 (16-62)	43.8 (16-72)	45.1 (15-75)
	x xx xxx			n.s.
Mean immobilisation time (weeks) and range	9.4 (1-30)	4.0 (3-12)	9.6 (1-53)	6.3 (2-16)
<u>Type of fracture</u>				
Compound	1	1	3	0
Dislocated	23	4	34	22
<u>End result of treatment</u>				
Good	21	6	42	52
Fair	5	2	11	8
Poor	0	0	0	3

n.s = not significant

x = $p < 0.05$
 xx = $p < 0.01$
 xxx = $p < 0.001$

Median age at the time of fracture was 38 years (range 15-75) and the median follow-up time 108 months (range 93-126). During the treatment of fracture only one patient (with femoral fracture) had clinically suspected and phlebographically proven DVT. Four patients had symptoms of pulmonary embolism during the fracture treatment, but in no case was this verified objectively nor could a DVT be demonstrated. These five patients were all treated with oral anticoagulants for three to six months. Data about the fractured legs are presented in Table 1.

Fractures were analysed in four groups: femoral fractures (26), condylar fractures (8), fractures of the lower leg (53) and malleolar fractures (63). As can be seen from Table 1 the mean age was higher the more distal the fracture, but the mean immobilisation time did not differ significantly between the groups. At follow up the end result of fracture treatment was estimated from the clinical findings and subjective complaints of the patients. The end result of fracture treatment was considered good when the patient had no sequelae, fair when the patient had some complaints from the leg but had normal or near normal function and poor when the activity was reduced because of symptoms from the leg. Presence of dislocation was based on x-ray appearance.

At follow up the patient records were reviewed. The patient answered a questionnaire concerning the subjective manifestations of venous disorders of the limbs during the follow-up period and the present state of health. All patients were examined clinically. Presence of varicose veins, crural eczema, discoloration, swelling and leg ulcers were looked for.

"Clinical" DVI was considered present when the patient had had leg ulcer during the follow-up period and/or at least two symptoms or signs of venous insufficiency (swelling, discoloration, crural eczema or constant need for pressure bandage or support hose).

Venous occlusion strain gauge plethysmography was performed according to Hallböök et al (1970, 1971) in 299 limbs. The parameters used in the evaluation were reserve venous volume (RVV) in ml/100 ml tissue and maximum venous emptying (MVE) in ml/100 ml tissue/minute. RVV less than 1.5 and MVE less than 30 were classified as pathologic.'

Ambulatory venous pressure measurements were performed in 274 limbs. A dorsal foot vein was punctured percutaneously with a scalp vein needle and connected to a pressure transducer. The pressure fall and return time (from termination of exercise to restitution of pre-exercise pressure) were registered. The superficial veins were occluded during measurements with a rubber tourniquet applying a slight pressure in order to avoid superficial venous insufficiency to interfere with the results. A pressure fall of less than 30 mmHg and return time less than 25 seconds were regarded as abnormal (Pollack and Wood 1949, DeCamp et al 1951, Kreisman 1974).

In 293 limbs venous valve insufficiency was also recorded with the doppler ultrasound technique in the femoral and popliteal veins as described by Barnes (1982).

"Objective" DVI was considered present when the plethysmography showed impaired outflow (MVE <30 ml/100 ml tissue/min) and/or venous pressure measurements showed valvular insufficiency (return time < 25 sec) and/or the doppler recording showed insufficiency in the femoral or popliteal vein.

Arterial circulation was evaluated with the doppler technique and the arterial ankle/arm pressure index was measured. An index above 0.95 was regarded as normal.

For the statistical evaluation the chi-square method with Yates correction and Student's t-test were used.

Table 2

Results of questionnaire and clinical examination

	Fractured legs ¹⁾		Uninjured legs	
	No	percentage	No	percentage
Total no of legs	150		150	
<u>Questionnaire</u>				
Treated for DVT during follow-up	3	2.0	3	2.0
Operated during follow-up	58	38.7	59	39.3
Varicose veins	20	13.3	17	11.3
Leg ulcer during follow-up	7 ^x	4.7	1	0.6
Swollen leg	41 ^{xxx}	27.3	17	11.3
Eczema of leg	8	5.3	5	3.3
Discoloration	22	14.7	18	12.0
Constant need of compression/ support hose	5	3.3	1	0.6
<u>Clinical findings</u>				
Leg ulcer (active)	0		0	
Swollen leg	17 ^x	11.3	7	4.7
Venous eczema	11	7.3	6	4.0
Discoloration	40	26.6	36	24.0
Varicose veins	84	56.0	79	52.7
"Clinical" DVI	38 ^x	25.3	20	13.3

1) Differences from the uninjured side expressed as ^x=p<0.05,
^{xxx}=p<0.001

Table 3

Results of objective measurements of DVI

	Fractured legs ¹⁾		Uninjured legs	
	No	percentage	No	percentage
Total no of legs	150		150	
<u>Plethysmography</u>				
Total studied	150		149	
RVV < 1.5 ml/100 ml tissue	19	12.7	27	18.1
MVE < 30 ml/100 ml tissue/min	28	18.7	24	16.1
<u>Venous pressure</u>				
Total studied	138		136	
Return time < 25 sec	24	17.4	20	14.7
<u>Doppler</u>				
Total studied	147		146	
Insuff femoral vein	10	6.8	6	4.1
Insuff popliteal vein	14	9.5	10	6.8
Insuff fem and/or pop vein	20	13.6	14	9.6
"Objective" DVI	52	34.7	44	29.3

1) None of the differences from the uninjured side was significant

Results:

Results were recorded for each leg separately.

In Table 2 and 3 results in the fractured limbs are compared with the uninjured limbs. The statistically significant differences are few. More fractured legs were swollen and had leg ulcers during the follow up. "Clinical" DVI was more common in fractured legs than in uninjured. In objectively measured parameters there were no differences at follow up.

When the four different types of fractures were compared, "clinical" and "objective" DVI did not differ between the groups.

The effect of immobilisation on development of DVI was studied. Legs immobilised less than eight weeks (106 legs) were compared to legs immobilised more than eight weeks (44 legs). "Objective" DVI did not differ between the groups. The detected DVT during fracture treatment and the clinically suspected pulmonary emboli were all in patients with long immobilisation.

"Clinical" and "objective" DVI did not differ between legs with dislocated and undislocated fractures. However, outflow obstruction was more common in limbs with undislocated fractures ($p < 0.05$) while insufficiency, as measured with doppler, was more common in legs with dislocated fractures ($p < 0.001$). Femoral fractures were relatively more common in the groups with dislocation while malleolar fractures were more commonly undislocated.

The influence of age on development of DVI is presented in Table 4. The pattern of fractures was alike in patients over and under 45 years of age. Both "clinical" and "objective" DVI was more common in the older age group. Comparing legs with and without fractures in the

different age groups no differences could be demonstrated except that "clinical" DVI was more common in fractured legs than in not fractured legs in the younger age group.

Table 4

DVI related to age

	Age < 45 years (89 pat)		Age > 45 years (61 pat)	
	Fractured legs	Uninjured legs	Fractured legs	Uninjured legs
"Clinical" DVI	10/89 └─ x ─┐ └─ xxx ─┐ └─ ─┐ └─ xxx ─┐	2/89	28/61	18/61
<u>Plethysmography</u>				
MVE <30 ml/100 ml tissue/min	16/89	15/89	12/61	9/61
<u>Venous pressure</u>				
Ret time < 25 sec	4/84 └─ ─┐ └─ xxx ─┐ └─ ─┐ └─ xxx ─┐	2/75	20/57	18/60
<u>Doppler</u>				
Insuff fem vein	1/89 └─ ─┐ └─ xx ─┐	2/89	9/57	4/59
Insuff pop vein	3/89 └─ ─┐ └─ xx ─┐ └─ ─┐ └─ xx ─┐	1/89	11/57	9/59
Insuff fem and/or pop vein	4/89 └─ ─┐ └─ xxx ─┐ └─ ─┐ └─ xx ─┐	3/89	16/57	11/59
"Objective" DVI	18/89 └─ ─┐ └─ xxx ─┐ └─ ─┐ └─ xx ─┐	17/89	34/61	27/61

The frequency of both "clinical" and "objective" DVI was significantly higher ($p < 0.001$) in legs with fair end result of fracture treatment compared to legs with good end results. The frequency of venous outflow obstruction ($MVE < 30$) was the same in both groups while valvular insufficiency, as measured both with venous pressure measurements and doppler, was significantly higher in legs with fair end result of fracture treatment.

The significance of the popliteal vein valves in development of DVI is presented in Table 5. There was no difference in frequency of fractured legs between legs with and without insufficiency of the popliteal vein as measured with doppler. Both "clinical" DVI, pathologic return time in venous pressure recordings and insufficiency of the femoral vein were significantly more common in legs with insufficiency in the popliteal vein compared to legs with normal popliteal vein. Six of eight limbs with leg ulcer during the follow up period had insufficiency in the popliteal vein.

In 112 legs an arterial ankle/arm index less than 0.95 were registered. No leg had an index less than 0.6. There were no differences in DVI "clinically" or "objectively" between legs with pathologic and normal arterial index although patients with index less than 0.95 were somewhat older.

Discussion

Damage of the deep veins and development of deep venous thrombosis is frequent after lower limb trauma (Nylander and Semb 1972, Hjelmstedt and Bergvall 1968). Bauer (1944) reported an 11 per cent incidence of clinically detected DVI after leg injuries of various kind. He concluded that DVI was twelve times as common after leg injury as in legs with DVI from other causes.

A few studies of phlebographically detected late changes

Table 5

DVI in relation to sufficiency of popliteal vein as recorded by doppler.

	Insufficiency of popliteal vein 1)	Normal popliteal vein
Total no of legs	24	269
No of fractured legs	14	133
Type of fracture:		
femoral	6	20
condylar	0	7
lower leg	6	47
malleolar	2	59
"Clinical" DVI	16 ^{xxx}	43
<u>Plethysmography</u>		
MVE <30 ml/100 ml tissue/min	1/24	48/269
<u>Venous pressure</u>		
Ret time <25 sec	15/24 ^{xxx}	27/235
<u>Doppler</u>		
Insuff fem vein	5/24 ^{xx}	11/269
MVE < 30 and/or ret time <25	15 ^{xxx}	69

1) Differences from the normal side expressed as

xx = $p < 0.01$ and xxx = $p < 0.001$

of the deep veins after fracture of the lower extremity have been performed. In legs with thrombosis after tibial fractures Bergvall and Hjelmstedt (1968) found that recanalization was a slow process, as a rule requiring 3-4 years. Recanalization was slower the more distal the thrombosis was localized. Miehle (1982) found phlebographic postthrombotic changes in 39 per cent of extremities with compound lower-leg fractures 6 months to eight years previously.

Deep venous insufficiency developing after fractures has been poorly investigated. Støren and Auensen (1971) made a clinical evaluation of 52 patients with thrombosis after hip fracture 1-32 months (average 16 months) after injury. They found oedema in 48 per cent, induration of skin in 21 per cent and leg ulcer in 2 per cent, 79 per cent of the patients had no subjective complaints. Willen et al (1982) examined 38 patients with tibial fractures 13-17 years previously using clinical examination and directional doppler technique and in some cases phlebography. At the follow up, 15 patients (40 per cent) had symptoms of DVT and in 8 patients (21 per cent) objective venous insufficiency was established. High energy trauma, long immobilisation and age over 45 years were significantly associated with venous insufficiency at follow up. Miehle (1982) in his follow-up 6 months to eight years after compound lower leg fractures found constant swelling of the leg in 13 per cent, eczema in 9 per cent, pigmentation in 29 per cent and leg ulcer in 3 per cent.

In contrast to the previous studies we evaluated also the uninjured limbs and found very few differences at follow-up between the injured and uninjured limbs. "Clinical" DVI was more common in fractured limbs but "objective" DVI was not. We could not show any difference on development of DVI, "clinical" or "objective", in relation to different types of fractures. A long immobilisation time did not affect the development of "objective"

DVI. Limbs with dislocated fracture showed significantly more venous valve damages as measured with doppler but the limbs with undislocated fracture showed more outflow obstruction. "Clinical" and "objective" DVI did not differ significantly between groups.

Age seems to be one of the most important factors for development of DVI (Lindhagen et al 1983 and Lindhagen et al accepted for publication). DVI was highly significantly more common in patients over 45 years of age than in younger patients both in fractured legs and uninjured legs.

The importance of the valve in the popliteal vein for development of DVI has been pointed out by Shull et al (1979). Ulceration did not occur in their study, even in the presence of femoral vein occlusion, if the popliteal valves were competent. Our results support their findings as do earlier studies from our group (Lindhagen et al 1983, Lindhagen et al accepted for publication).

In legs with insufficiency of the popliteal veins as measured by doppler both "clinical" DVI, pathologic venous pressure and insufficiency of the femoral vein was significantly more common than in legs with normal popliteal vein. Of the eight legs with leg ulcer during follow up six had insufficiency in the popliteal vein.

In conclusion this study shows that "clinical" symptoms of DVI are more common in fractured legs than in uninjured ones, while objectively diagnosed DVI does not differ between the groups. High age and incompetence of the popliteal valve seem to be more important in the development of DVI than earlier fracture. The type of fracture seems to affect the development of DVI to a minor extent.

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LATE VENOUS FUNCTION IN THE LEG AFTER DEEP VENOUS
THROMBOSIS OCCURRING IN RELATION TO PREGNANCY

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ABSTRACT

23 patients, who had developed an objectively diagnosed deep venous thrombosis (DVT) during pregnancy or the first week after delivery, were investigated 3 - 13 years later (mean 7 years) to evaluate the frequency of deep venous insufficiency (DVI). The evaluation included clinical examination, registration of subjective complaints and objective measurements with plethysmography, venous pressure and doppler ultrasound.

At follow-up there were clinical signs or subjective complaints of DVI in eight legs with earlier DVT (35%) as compared to none in the non-thrombosed contralateral legs. Objective evidence of DVI was present in 15 of the earlier thrombosed legs (65%) as compared to 5 in the non-thrombosed legs (22%). The differences between thrombosed and non-thrombosed legs are significant. No correlation between objectively measured DVI and extent of the DVT could be seen.

It is concluded that a DVT during pregnancy often leads to DVI and the risk seems higher than after DVT occurring in other groups of patients.

INTRODUCTION

Deep venous thrombosis (DVT) is an uncommon but feared complication of pregnancy. It presents both diagnostic and therapeutic problems. The incidence has been estimated to be two to five per 1 000 deliveries (Bonnar 1981) and pulmonary embolism is the second most common cause of maternal mortality (Editorial Br Med J 1979, Bonnar 1981).

The incidence of deep venous insufficiency (DVI) after DVT presenting during pregnancy has been considered high (Gjöres 1956) but is not known.

The aim of this study was to establish the frequency of both clinically detected and objectively measured venous insufficiency after DVT developed during pregnancy and to make a comparison with the unthrombosed leg.

MATERIAL

In a prospective study 1974 - 1980 DVT was objectively diagnosed in relation to pregnancy in 13 patients at Kärnsjukhuset, Skövde (Bergqvist et al 1983). Ten of these patients could be reached for follow-up in the present study. In 1971 -1979 eighteen patients at Allmänna sjukhuset, Malmö had objectively diagnosed DVT during pregnancy and thirteen of them could be reached for follow-up. The material thus consists of 23 patients with a median age at the time of DVT of 27 years (range 18 -41 years). Mean, as well as median, follow-up time was 7 years (range 3 - 13 years). The DVT appeared in the first trimester in 4 patients, in the second in 3 patients and in the third in 7 patients. In nine patients the DVT was diagnosed in the first week after delivery but in five cases the symptoms had started before delivery. Eleven patients had their DVT during their first pregnancy.

In all patients the DVT was objectively diagnosed (phle-

bography in 21 patients and the combination of plethysmography and thermography (Watz et al 1979) in two).

The DVT was left-sided in nineteen patients (83%). No patient had had a bilateral DVT. The extension of the DVT's is shown in Table 1. Six patients had isolated ileofemoral thrombosis. Two patients were not phlebographed why the extension of the DVT is not known. However, both had plethysmographic signs of iliac vein obstruction. No pulmonary emboli were noted.

All patients were treated with heparin during pregnancy. After delivery they were given heparin (if lactating) or oral anticoagulants, and during labor and delivery dextran was given. Nineteen patients were treated for one to four months after delivery while four patients had a shorter period of treatment. No patient was operated for the thrombosis.

Twelve patients became pregnant once again during the follow-up period. During these subsequent pregnancies six patients were treated prophylactically with heparin and five were treated with dextran during the delivery only. One patient had an induced abortion of fear for developing a new DVT. No prophylactic treatment was given in that case. No thrombosis was noted during these pregnancies.

Three patients had earlier had clinically suspected but not objectively verified thrombosis.

METHODS

At follow-up the patients answered a questionnaire concerning subjective manifestations of venous disorders in the leg during the follow-up period and their present state of health. All examinations were made of both the thrombosed leg ("DVT" leg) and the contralateral non-

thrombosed leg. Clinical examination considered presence of leg ulcers, swelling, crural excema, discoloration and varicose veins.

"Clinical" DVI was considered present when a patient had had a venous leg ulcer after the DVI and/or at least two symptoms or signs of venous insufficiency (swelling, discoloration, crural excema, nightly cramps or need for constant pressure bandage or compression stocking).

Venous occlusion strain-gauge plethysmography was performed (Hallböök et al 1970, Hallböök & Göthlin 1971). The parameters used in the evaluation were reserve venous volume (RVV) in ml/100 ml tissue and maximum venous emptying (MVE) in ml/100 ml tissue and minute. RVV less than 1,5 and MVE less than 30 were classified as pathologic (Hallböök & Göthlin 1971). A biphasic venous emptying indicating isolated iliac obstruction was especially looked for (Bergqvist & Hallböök 1979).

Ambulatory venous pressure measurements were performed. A dorsal foot vein was percutaneously catheterized with a scalp vein needle and connected to a pressure transducer. The pressure fall and return time (from termination of exercise to restitution of pre-exercise pressure) were registrated. The superficial veins were occluded during measurements with a rubber tourniquet with slight pressure to avoid superficial venous insufficiency to interfere with the results. A pressure fall of less than 30 mmHg and return time less than 25 seconds were regarded as abnormal (DeCamp et al 1951, Pollack & Wood 1949, Shull et al 1979). Doppler ultrasound was used to record venous valve insufficiency in the femoral and popliteal vein as described by Barnes (1982).

"Objective" DVI was considered present when plethysmography showed impaired venous outflow from the leg indicating obstruction (MVE less than 30 ml/100 ml/min) and/or venous pressure indicated deep venous reflux

(return time less than 25 spec) and/or doppler ultrasound indicated venous valvular insufficiency.

The arterial circulation was determined in each patient with doppler ultrasound technique and the ankle/arm arterial pressure index calculated. An index over 0,9 was regarded as normal.

For statistical calculations the chi-square method with Yates correction was used. Significance was considered when $p < 0,05$.

RESULTS

Results were recorded for each leg separately.

"Clinical" DVI was present in eight "DVT"-legs (35%). In seven legs both clinical signs and subjective symptoms were present while one patient only had subjective complaints. No non-thrombosed leg had "clinical" DVI ($p < 0,01$). No correlation between "clinical" DVI and extent of DVT was observed. Eight "DVT"-legs and six non-thrombosed legs had varicose veins at the clinical examination. Three patients had bilateral varicose veins. Two patients had had leg ulcer during the follow-up period. One had a DVT in the whole leg, including the iliac vein, and the other a DVT in the lower leg and into the distal part of the femoral vein.

Results of objective tests for DVI are presented in Table I. Fifteen "DVT"-legs (65%) had "objective" DVI as compared to five non-thrombosed legs (22%), ($p < 0,01$). Seven of these fifteen legs had "clinical" DVI as well. One "DVT"-leg had "clinical" DVI without "objective" DVI. Of the five patients with "objective" DVI in the healthy leg three had "objective" DVI in the contralateral thrombosed leg.

TABLE I
Extension of DVT's and results at follow-up.

[illegible]

In six legs the diagnosis of "objective" DVI was based only on venous outflow obstruction (MVE <30), in two legs on pathologic venous pressure return time only, in two on insufficiency in the femoral vein only and in the remainder on insufficiency of the popliteal vein only or in combination with other signs of "objective" DVI.

No correlation between "objective" DVI and the extension of the DVT was seen. Follow-up time did not differ between legs with "objective" DVI and legs without (89 vs. 85 months) nor did the length of treatment for the DVT.

Ten patients had been examined with plethysmography 1 - 3 months after delivery. The "DVT"-leg was pathologic with impaired venous outflow in five cases. None showed a biphasic emptying pattern. Four of the five legs with a pathological control plethysmogram had "objective" DVI at follow-up, while this was found in only two legs with normal control plethysmography.

All patients had a normal arterial ankle/brachial pressure index at follow-up.

DISCUSSION

The incidence of objectively diagnosed DVT in Sweden has been estimated to 0,07% of full term pregnancies (Bergqvist et al 1983), and in Great Britain to 2-5 per 1000 deliveries (Bonnar 1981). Although the incidence is low, pulmonary embolism is the second most common cause of maternal mortality (Editorial Br Med J 1979, Bonnar 1981). Diagnosis of DVT during pregnancy presents special problems since radiation should be avoided. The treatment of choice is heparin since it does not cross the placental barrier (Bonnar 1976). The frequency of DVI after a DVT presenting during pregnancy has been considered high (Gjöres 1956) but has not been studied with objective test methods before, and not in materials where

objective criteria of DVT had been used.

The present study shows a frequency of 65% of objectively measured venous insufficiency after a mean follow-up period of seven years. This follow-up period should be adequate for DVI to develop (Shull et al 1979). The frequency is higher than after postoperative DVT detected with the fibrinogen uptake test (Lindhagen et al 1984) or after clinically suspected DVT diagnosed with phlebography (Lindhagen et al, accepted for publication). Objectively measured DVI in these groups have been 32% and 49% respectively. It should be pointed out, however, that the study on fibrinogen detected postoperative DVT was completely prospective with sensitive screening of DVT, the study on phlebographically diagnosed DVT's was retrospective, and the present study is mostly retrospective and objective diagnoses of DVT with phlebography may have been avoided for fear of radiation injuring the fetus.

No correlation between the extent of the DVT and the presence of "objective" DVI at follow-up could be found. This is in accordance with earlier results from our group (Lindhagen et al 1984, Lindhagen et al, accepted for publication). Left-sided thrombosis dominated in this study and a high frequency of iliac vein thrombi was seen as in other studies of DVT during pregnancy (Bergqvist et al 1983, Bergqvist & Hedner 1983). This distribution of DVT's is also seen in patients with DVT in relation to intake of oral contraceptives (Bergqvist et al 1982). That this left-sided dominance influences the development of DVI seems unlikely since we have not found any correlation between DVI and side-localization of DVT in earlier studies (Lindhagen et al 1984, Lindhagen et al, accepted for publication).

"Clinical" DVI was less common than "objective" DVI. Subjective symptoms of DVI are actually indications of complications after a deep venous insufficiency, e.g.

swelling or leg ulcer, and they will appear later than the objectively measured venous insufficiency (Barnes et al 1973, Lawrence & Kakkar 1980).

A frequency of 22% of "objectively" measured DVI was found in the non-thrombosed legs. This is somewhat less than we have observed in other studies (Lindhagen et al 1984, Lindhagen et al, accepted for publication) where the frequency was about 30%. This might be due to the patients in this study being relatively young, since one explanation of DVI in seemingly healthy legs is aging of the venous valves (Kistner 1980). In earlier studies we also found a correlation between frequency of DVI and age (Lindhagen et al 1984, Lindhagen et al, accepted for publication).

This material is small because of the relative infrequency of DVI during pregnancy, and because of our demand to accept only objectively diagnosed DVT. Nonetheless the results indicate that DVT in relation to pregnancy frequently leads to DVI and the risk may be even higher than after DVT in other groups of patients. Since the patients are young they are at high risk of disabling DVI during many years. The risk of pulmonary embolism must not be forgotten. As a consequence of these findings we recommend that objective diagnosis should be carried out on the slightest suspicion of DVT in relation to pregnancy. Non-invasive methods should be used as far as possible, but when they are not conclusive, phlebography is indicated.

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